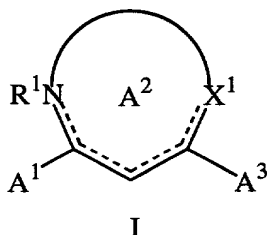


**What Is Claimed Is:**

1. A compound of Formula I:



in which:

the dashed lines indicate optional unsaturation without violating valency rules;

$R^1$  is hydrogen,  $(C_{1-6})$ alkyl or  $-C(O)R^6$ , wherein  $R^6$  is as defined below, or  $R^1$  is absent when a double bond exists between the nitrogen atom to which  $R^1$  is attached and an adjacent ring atom or  $R^1$  is as defined below;

$X^1$  is  $-NR^2$ -,  $-S$ -,  $-S(O)$ -,  $-S(O)_2$ - or  $-O$ -, wherein  $R^2$  is hydrogen or  $(C_{1-6})$ alkyl or is absent when a double bond exists between the nitrogen atom to which  $R^2$  is attached and an adjacent ring atom;

$A^1$  is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, or  $A^1$  together with  $R^1$  and the atoms to which  $A^1$  and  $R^1$  are attached forms a fused polycyclic ring system selected from heteroaryl and unsaturated, partially unsaturated or saturated heterocycloalkyl in any case containing a total of 10 to 15 ring atoms, wherein  $A^1$  may be substituted with a group selected from  $-X^2R^3$ ,  $-X^2OR^3$ ,  $-X^2C(O)R^3$ ,  $-X^2OC(O)R^3$ ,  $-X^2C(O)OR^3$ ,  $-X^2SR^3$ ,  $-X^2S(O)R^3$ ,  $-X^2S(O)_2R^3$ ,  $-X^2NR^3R^4$ ,  $-X^2NR^4C(O)R^3$ ,  $-X^2NR^4C(O)OR^3$ ,  $-X^2C(O)NR^3R^4$ ,  $-X^2NR^4C(O)NR^3R^4$ ,  $-X^2NR^4C(NR^4)NR^3R^4$ ,  $-X^2NR^4S(O)_2R^3$  and  $-X^2S(O)_2NR^3R^4$ , wherein  $X^2$  is a bond or  $(C_{1-6})$ alkylene,  $R^3$  is  $-X^2R^5$  wherein  $X^2$  is as defined above and  $R^5$  is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10

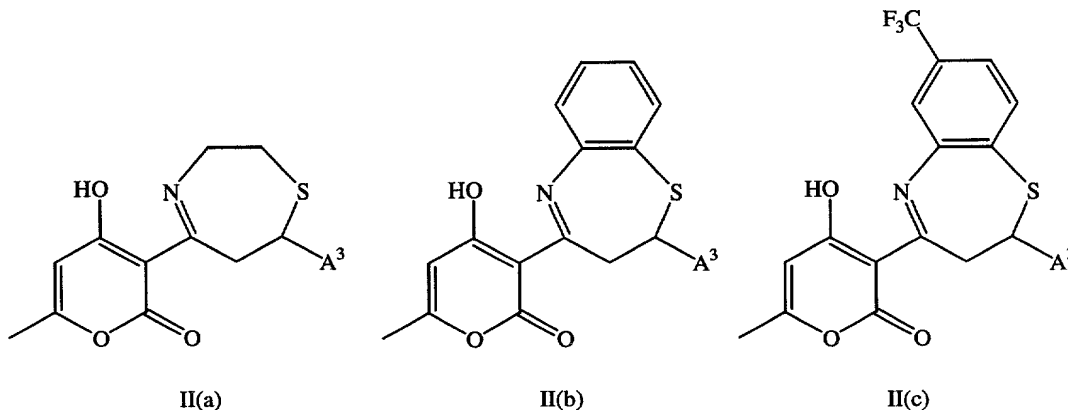
ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and  $R^4$  at each occurrence independently is hydrogen,  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-6})$ alkyl, wherein each ring within  $A^1$  and  $R^5$  contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from  $(C_{1-6})$ alkyl, cyano, halo, nitro, halo-substituted  $(C_{1-6})$ alkyl,  $-X^2OR^4$ ,  $-X^2C(O)R^6$ ,  $-X^2OC(O)R^6$ ,  $-X^2C(O)OR^4$ ,  $-X^2SR^4$ ,  $-X^2S(O)R^6$ ,  $-X^2S(O)_2R^6$ ,  $-X^2NR^4R^4$ ,  $-X^2NR^4C(O)R^6$ ,  $-X^2NR^4C(O)OR^4$ ,  $-X^2C(O)NR^4R^4$ ,  $-X^2NR^4C(O)NR^4R^4$ ,  $-X^2NR^4C(NR^4)NR^4R^4$ ,  $-X^2NR^4S(O)_2R^6$  and  $-X^2S(O)_2NR^4R^4$ , wherein  $X^2$  and  $R^4$  are as defined above and  $R^6$  is  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-6})$ alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within  $A^1$  and  $R^5$  may be substituted further with 1 to 2 groups independently selected from  $(C_{1-6})$ alkylidene, oxo, imino and thioxo, with the proviso that only one of  $A^1$  and  $R^5$  is a fused polycyclic ring system;

$A^2$  is a monocyclic or fused bicyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein  $A^2$  may be substituted with a group selected from  $-X^2R^8$ ,  $-X^2OR^8$ ,  $-X^2C(O)R^8$ ,  $-X^2OC(O)R^8$ ,  $-X^2C(O)OR^8$ ,  $-X^2SR^8$ ,  $-X^2S(O)R^8$ ,  $-X^2S(O)_2R^8$ ,  $-X^2NR^4R^8$ ,  $-X^2NR^4C(O)R^8$ ,  $-X^2NR^4C(O)OR^8$ ,  $-X^2C(O)NR^4R^8$ ,  $-X^2NR^4C(O)NR^4R^8$ ,  $-X^2NR^4C(NR^4)NR^4R^8$ ,  $-X^2NR^4S(O)_2R^8$  and  $-X^2S(O)_2NR^4R^8$ , wherein  $X^2$  is a bond or  $(C_{1-6})$ alkylene,  $R^8$  is  $-X^2R^9$  wherein  $X^2$  is as defined above and  $R^9$  is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and  $R^4$  at each occurrence independently is hydrogen,  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-6})$ alkyl, wherein each ring within  $A^2$  and  $R^8$  contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from  $(C_{1-6})$ alkyl, cyano, halo, nitro, halo-substituted  $(C_{1-6})$ alkyl,  $-X^2OR^4$ ,  $-X^2C(O)R^6$ ,  $-X^2OC(O)R^6$ ,  $-X^2C(O)OR^4$ ,  $-X^2SR^4$ ,  $-X^2S(O)R^6$ ,  $-X^2S(O)_2R^6$ ,  $-X^2NR^4R^4$ ,  $-X^2NR^4C(O)R^6$ ,  $-X^2NR^4C(O)OR^4$ ,  $-X^2C(O)NR^4R^4$ ,

-X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>X<sup>2</sup>C(O)OR<sup>4</sup>,  
 -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>6</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>4</sup>, wherein X<sup>2</sup> and R<sup>4</sup> are as defined above and  
 R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, and wherein any said  
 heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within A<sup>2</sup> and R<sup>8</sup>  
 may be substituted further with 1 to 2 groups independently selected from  
 (C<sub>1-6</sub>)alkylidene, oxo, imino and thioxo, with the proviso that only one of A<sup>2</sup> and  
 R<sup>8</sup> is a fused polycyclic ring system; and

A<sup>3</sup> is a monocyclic or fused polycyclic ring system selected from aryl  
 containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14  
 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or  
 heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A<sup>3</sup> may  
 be substituted with a group selected from -X<sup>2</sup>R<sup>9</sup>, -X<sup>2</sup>OR<sup>9</sup>, -X<sup>2</sup>C(O)R<sup>9</sup>,  
 -X<sup>2</sup>OC(O)R<sup>9</sup>, -X<sup>2</sup>C(O)OR<sup>9</sup>, -X<sup>2</sup>SR<sup>9</sup>, -X<sup>2</sup>S(O)R<sup>9</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>9</sup>,  
 -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>9</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>9</sup>,  
 -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>9</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>9</sup>, wherein X<sup>2</sup> is a bond  
 or (C<sub>1-6</sub>)alkylene, R<sup>9</sup> is -X<sup>2</sup>R<sup>10</sup> wherein X<sup>2</sup> is as defined above and R<sup>10</sup> is aryl  
 containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10  
 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or  
 heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R<sup>4</sup> at each  
 occurrence independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl,  
 wherein each ring within A<sup>3</sup> and R<sup>10</sup> contains from 3 to 8 ring atoms and may be  
 substituted with 1 to 3 groups independently selected from (C<sub>1-6</sub>)alkyl, cyano,  
 halo, nitro, halo-substituted (C<sub>1-6</sub>)alkyl, -X<sup>2</sup>OR<sup>4</sup>, -X<sup>2</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>OC(O)R<sup>6</sup>,  
 -X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>SR<sup>4</sup>, -X<sup>2</sup>S(O)R<sup>6</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>6</sup>,  
 -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>4</sup>,  
 -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>6</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>4</sup>, wherein X<sup>2</sup> and R<sup>4</sup> are as defined above and  
 R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, and wherein any said  
 carbocycloalkyl and heterocycloalkyl rings within A<sup>3</sup> and R<sup>10</sup> may be substituted  
 further with 1 to 2 groups independently selected from (C<sub>1-6</sub>)alkylidene, oxo,  
 imino and thioxo, with the proviso that only one of A<sup>3</sup> and R<sup>10</sup> is a fused

polycyclic ring system; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof; with the proviso that when said compound is selected from the group consisting of Formulae II(a), II(b) and II(c):



then A<sup>3</sup> is other than:

- unsubstituted pyridyl;
- unsubstituted thienyl;
- unsubstituted indolyl;
- unsubstituted phenyl;
- benzo[1,3]dioxolyl;
- 2,3-dihydro-benzo[1,4]dioxinyl;
- phenyl which is mono-substituted by fluoro, bromo, iodo, nitro, methyl, isopropyl, ethoxy or methylsulfanyl; and
- phenyl which is substituted by at least one of chloro, hydroxy or methoxy.

2. The compound of claim 1, and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts of said compound, with the further proviso that A<sup>3</sup> is other than:

- unsubstituted pyridyl;
- unsubstituted thienyl;

unsubstituted indolyl;

unsubstituted phenyl;

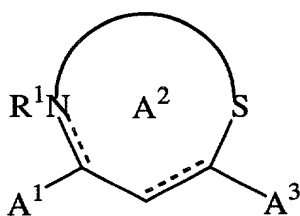
benzo[1,3]dioxolyl;

2,3-dihydro-benzo[1,4]dioxinyl; and

phenyl which is substituted by at least one of halogen, nitro, hydroxy, (C<sub>1-3</sub>)alkyl, methoxy, ethoxy and methylsulfanyl.

3. The compound of claim 1, and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts of said compound, with the further proviso that A<sup>1</sup> is not 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl.

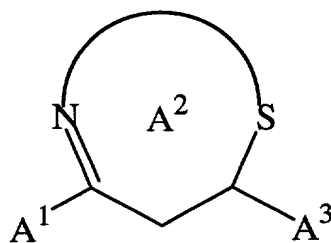
4. The compound of Claim 1 in which said compound is of Formula I(A):



I(A)

in which R<sup>1</sup>, A<sup>1</sup>, A<sup>2</sup> and A<sup>3</sup> are as defined in Claim 1; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

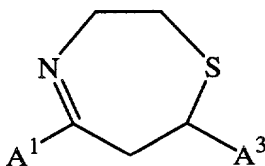
5. The compound of Claim 4 in which said compound is of Formula I(B):



I(B)

in which R<sup>1</sup>, A<sup>1</sup>, A<sup>2</sup> and A<sup>3</sup> are defined as in Claim 1; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

6. The compound of Claim 5 in which said A<sup>2</sup> is 2,3,6,7-tetrahydro-[1,4]thiazepin-5,7-ylene, that is the compound of Formula I(C):



I(C)

in which A<sup>1</sup> and A<sup>3</sup> are defined as in Claim 1, and said 2,3,6,7-tetrahydro-[1,4]thiazepin-5,7-ylene may be substituted with 1 to 3 groups independently selected from (C<sub>1-6</sub>)alkyl, cyano, halo, nitro, halo-substituted (C<sub>1-6</sub>)alkyl, -X<sup>2</sup>OR<sup>4</sup>, -X<sup>2</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>OC(O)R<sup>6</sup>, -X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>SR<sup>4</sup>, -X<sup>2</sup>S(O)R<sup>6</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>6</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>4</sup>, wherein X<sup>2</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>4</sup> at each occurrence independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, and R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

7. The compound of Claim 6 in which A<sup>1</sup> is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

8. The compound of Claim 7 in which said compound is selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-ethyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3[7-(2-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(3-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(4-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-[3-(3-trifluoromethyl-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-[3-(3,4-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-[3-(3,5-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(3-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-{7-[5-(2-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(3-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(4-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

5 4-hydroxy-6-methyl-3-{7-[5-(2-chloro-5-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-[7-(4-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

10 3-[7-(1-benzenesulfonyl-1*H*-pyrrol-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(3-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

15 4-hydroxy-6-methyl-3-[7-(5-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(1-methyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

20 3-[7-(3-chloro-2-methyl-5-trifluoromethyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(2,4-difluoro-benzenesulfonyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-(7-[2,2']bithienyl-5-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

25 3-{7-[1-(3,5-dichloro-phenyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(4-chloro-phenyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

30 3-[7-(5-chloro-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;



4-hydroxy-6-methyl-3-[7-(6-*p*-tolylsulfanyl-imidazo[2,1-*b*]thiazol-5-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(4,5-dibromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methylsulfanyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-chloro-1-methyl-3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(4-trifluoromethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(bis-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-3-[7-(4-methanesulfonyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; and

3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-methoxy-6-methyl-pyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

9. The compound of Claim 6 in which A<sup>1</sup> is 4-hydroxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

10. The compound of Claim 9 in which said compound is selected from the group consisting of:

3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-  
4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-  
4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

5 3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-1,4]thiazepin-5-yl]-  
4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one; and

3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-1,4]thiazepin-5-yl]-  
4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives;  
and the pharmaceutically acceptable salts thereof.

11. The compound of Claim 6 in which A<sup>1</sup> is 2-hydroxy-6-oxo-  
cyclohex-1-enyl or 2-methoxy-6-oxo-cyclohex-1-enyl; and the *N*-oxide  
derivatives, prodrug derivatives, protected derivatives, individual stereoisomers  
and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

12. The compound of Claim 11 in which said compound is selected  
from the group consisting of:

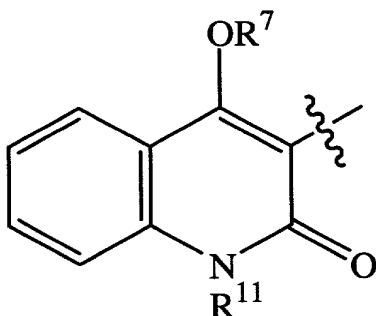
2-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-  
3-hydroxy-cyclohex-2-enone;

2-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-  
3-hydroxy-cyclohex-2-enone; and

3-hydroxy-2-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-  
[1,4]thiazepin-5-yl]-cyclohex-2-enone;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives;  
and the pharmaceutically acceptable salts thereof.

13. The compound of claim 6 in which A<sup>1</sup> is a group of Formula (c):



(c)

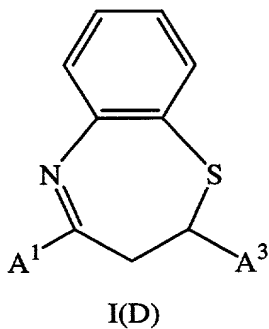
in which R<sup>7</sup> is hydrogen or methyl, R<sup>11</sup> is hydrogen or (C<sub>1-6</sub>)alkyl and the free valence is attached to A<sup>2</sup>; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

14. The compound of Claim 13 which is:

3-[7-2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-1*H*-quinolin-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

15. The compound of Claim 5 in which said A<sup>2</sup> is 2,3-dihydro-benzo[*b*][1,4]thiazepin-5,7-ylene that is the compound-of Formula I(D):



in which A<sup>1</sup> and A<sup>3</sup> are defined as in Claim 1, and said 2,3-dihydro-benzo[*b*][1,4]thiazepin-5,7-ylene may be substituted with 1 to 3 groups independently selected from (C<sub>1-6</sub>)alkyl, cyano, halo, nitro, halo-substituted (C<sub>1-6</sub>)alkyl, -X<sup>2</sup>OR<sup>4</sup>, -X<sup>2</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>OC(O)R<sup>6</sup>, -X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>SR<sup>4</sup>, -X<sup>2</sup>S(O)R<sup>6</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>6</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>4</sup>, wherein X<sup>2</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>4</sup> at each occurrence independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, and R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

16. The compound of Claim 15 in which A<sup>1</sup> is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

17. The compound of Claim 16 which is:

3-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-4-hydroxy-6-methyl-pyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

18. The compound of Claim 15 in which A<sup>1</sup> is 4-hydroxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

19. The compound of Claim 18 which is:

4-hydroxy-6-methyl-3-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-5,6-dihydro-pyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

20. The compound of Claim 15 in which A<sup>1</sup> is 2-hydroxy-6-oxo-cyclohex-1-enyl or 2-methoxy-6-oxo-cyclohex-1-enyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

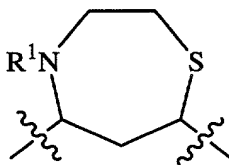
21. The compound of Claim 20 in which said compound is selected from the group consisting of:

3-hydroxy-2-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone; and

3-hydroxy-2-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

22. The compound of Claim 4 in which said A<sup>2</sup> is a group of Formula (k):



(k)

in which R<sup>1</sup> is defined as in Claim 1 and said group of Formula (k) may be substituted with 1 to 3 groups independently selected from (C<sub>1-6</sub>)alkyl, cyano, halo, nitro, halo-substituted (C<sub>1-6</sub>)alkyl, -X<sup>2</sup>OR<sup>4</sup>, -X<sup>2</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>OC(O)R<sup>6</sup>, -X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>SR<sup>4</sup>, -X<sup>2</sup>S(O)R<sup>6</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>6</sup>,

-X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>4</sup>,  
-X<sup>2</sup>C(O)NR<sup>4</sup>X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>6</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>4</sup>, wherein X<sup>2</sup> is a  
bond or (C<sub>1-6</sub>)alkylene, R<sup>4</sup> at each occurrence independently is hydrogen, (C<sub>1-6</sub>)  
alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, and R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted  
(C<sub>1-6</sub>)alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected  
derivatives, individual stereoisomers and mixtures of stereoisomers; and the  
pharmaceutically acceptable salts thereof.

23. The compound of Claim 22 in which R<sup>1</sup> is hydrogen; and the  
*N*-oxide derivatives, prodrug derivatives, protected derivatives, individual  
stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable  
salts thereof.

24. The compound of Claim 22 in which A<sup>1</sup> is 4-hydroxy-6-methyl-  
2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the  
*N*-oxide derivatives, prodrug derivatives, protected derivatives, individual  
stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable  
salts thereof.

25. The compound of Claim 24 in which said compound is selected  
from the group consisting of:

3-[4-acetyl-7-(2,4-dimethoxy-phenyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-  
methyl-pyran-2-one; and

3-[7-(2,4-dimethoxy-phenyl)-4-(2,2,2-trifluoro-ethanoyl)-[1,4]thiazepan-  
5-yl]-4-hydroxy-6-methyl-pyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives;  
and the pharmaceutically acceptable salts thereof.

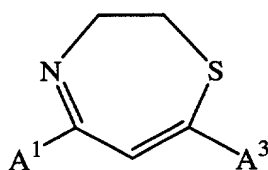
26. The compound of Claim 22 in which A<sup>1</sup> is optionally substituted  
phenyl.

27. The compound of Claim 26 which is:

1-[7-(2,4-dimethoxy-phenyl)-5-(3-fluoro-4-methoxyphenyl)-  
[1,4]thiazepan-4-yl]-ethanone;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives;  
and the pharmaceutically acceptable salts thereof.

28. The compound of Claim 4 in which said A<sup>2</sup> is 2,3-dihydro-  
[1,4]thiazepin-5,7-ylene that is the compound of Formula I(F):



I(F)

in which A<sup>1</sup> and A<sup>3</sup> are defined as in Claim 1, and said 2,3-dihydro-  
[1,4]thiazepin-5,7-ylene may be substituted with 1 to 3 groups independently  
selected from (C<sub>1-6</sub>)alkyl, cyano, halo, nitro, halo-substituted (C<sub>1-6</sub>)alkyl, -X<sup>2</sup>OR<sup>4</sup>,  
-X<sup>2</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>OC(O)R<sup>6</sup>, -X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>SR<sup>4</sup>, -X<sup>2</sup>S(O)R<sup>6</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>6</sup>,  
-X<sup>2</sup>NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>4</sup>,  
-X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>X<sup>2</sup>C(O)OR<sup>4</sup>,  
-X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>6</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>4</sup>, wherein X<sup>2</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>4</sup>  
at each occurrence independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, and R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl; and the *N*-oxide  
derivatives, prodrug derivatives, protected derivatives, individual stereoisomers  
and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

29. The compound of Claim 28 in which A<sup>1</sup> is 4-hydroxy-6-methyl-  
2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the  
*N*-oxide derivatives, prodrug derivatives, protected derivatives, individual  
stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable  
salts thereof.

30. The compound of Claim 29 in which said compound is selected from the group consisting of:

3-[7-(2,4-dimethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; and

3-(7-[2,2']bithienyl-5-yl-2,3-dihydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

31. The compound of Claim 28 in which A<sup>1</sup> is 4-hydroxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-5,6-dihydro-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

32. The compound of Claim 31 which is:

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

33. The compound of Claim 28 in which A<sup>1</sup> is 2-hydroxy-6-oxo-cyclohex-1-enyl or 2-methoxy-6-oxo-cyclohex-1-enyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

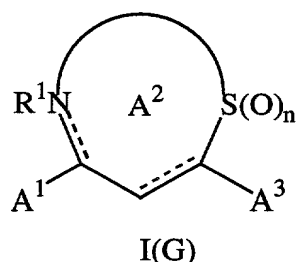


34. The compound of Claim 33 which is:

2-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

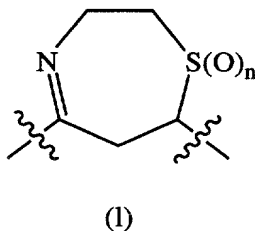
and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

35. The compound of Claim 1 in which said compound is of Formula I(G):



in which *n*, *R*<sup>1</sup>, *A*<sup>1</sup>, *A*<sup>2</sup> and *A*<sup>3</sup> are defined as in Claim 1; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

36. The compound of Claim 35 in which *A*<sup>2</sup> is a group of Formula (I):



in which *n*, and *R*<sup>1</sup> are defined as in Claim 1 and said group of Formula (I) may be substituted with 1 to 3 groups independently selected from (C<sub>1-6</sub>)alkyl, cyano, halo, nitro, halo-substituted (C<sub>1-6</sub>)alkyl, -X<sup>2</sup>OR<sup>4</sup>, -X<sup>2</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>OC(O)R<sup>6</sup>, -X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>SR<sup>4</sup>, -X<sup>2</sup>S(O)R<sup>6</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>6</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>4</sup>, wherein X<sup>2</sup> is a

bond or (C<sub>1-6</sub>)alkylene, R<sup>4</sup> at each occurrence independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, and R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

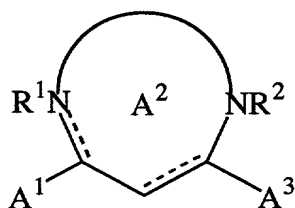
37. The compound of Claim 36 in which *n* is 1 and A<sup>1</sup> is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

38. The compound of Claim 37 which is:  
3-[7-(2,4-dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1*H*-1λ<sup>4</sup>-[1,4]thiazepin-5-yl]-4-hydroxy-6-methoxy-pyran-2-one;  
and the *N*-oxide derivatives, prodrug derivatives, protected derivatives; and the pharmaceutically acceptable salts thereof.

39. The compound of claim 36 in which *n* is 2 and A<sup>1</sup> is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

40. The compound of claim 39 which is:  
3-[7-(2,4-dimethoxy-phenyl)-1,1-dioxo-2,3,6,7-tetrahydro-1*H*-1λ<sup>6</sup>-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;  
and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

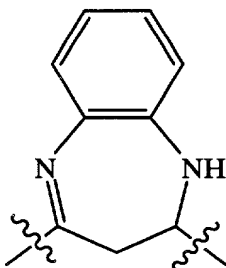
41. The compound of Claim 1 in which said compound is of Formula I(I):



I(I)

in which R¹, R², A¹, A² and A³ are as defined in Claim 1; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

42. The compound of Claim 41 in which said A² is a group of Formula (j):



(j)

in which said group of Formula (j) may be substituted with 1 to 3 groups independently selected from (C<sub>1-6</sub>)alkyl, cyano, halo, nitro, halo-substituted (C<sub>1-6</sub>)alkyl, -X²OR⁴, -X²C(O)R⁶, -X²OC(O)R⁶, -X²C(O)OR⁴, -X²SR⁴, -X²S(O)R⁶, -X²S(O)<sub>2</sub>R⁶, -X²NR⁴R⁴, -X²NR⁴C(O)R⁶, -X²NR⁴C(O)OR⁴, -X²C(O)NR⁴R⁴, -X²NR⁴C(O)NR⁴R⁴, -X²NR⁴C(NR⁴)NR⁴R⁴, -X²C(O)NR⁴X²C(O)OR⁴, -X²NR⁴S(O)<sub>2</sub>R⁶ and -X²S(O)<sub>2</sub>NR⁴R⁴, wherein X² is a bond or (C<sub>1-6</sub>)alkylene, R⁴ at each occurrence independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, and R⁶ is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

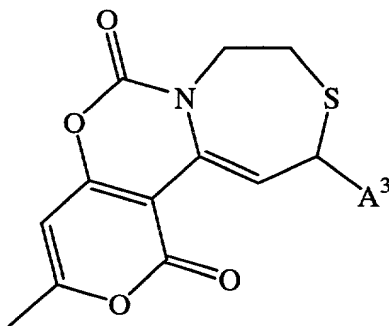
43. The compound of Claim 42 in which A<sup>1</sup> is 4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl or 4-methoxy-6-methyl-2-oxo-2*H*-pyran-3-yl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

44. The compound of Claim 43 which is:

3 - [ 4 - ( 2 , 4 - d i m e t h o x y - p h e n y l ) - 4 , 5 - d i h y d r o - 3 *H* - benzo[*b*][1,4]diazepin-2-yl] - 4-hydroxy-6-methylpyran-2-one;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

45. The compound of Claim 1 in which said compound is of Formula I(K):



I(K)

in which A<sup>3</sup> is defined as in Claim 1; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

46. The compound of claim 45 which is:

10-(2,4-dimethoxy-phenyl)-3-methyl-7,8-dihydro-10*H*-2,5-dioxa-9-thia-6*a*-aza-cyclohepta[*a*]naphthalene-1,6-dione;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives;  
and the pharmaceutically acceptable salts thereof.

47. A compound selected from the group consisting of:

4-hydroxy-3-[7-(2-methoxy-4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-  
[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

3-[7-(2-chloro-5-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-  
[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-2-methoxy-phenyl)-2,3,6,7-tetrahydro-  
[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-3-[7-(4-chloro-2-methoxy-phenyl)-2,3,6,7-tetrahydro-  
[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; and

4-hydroxy-3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-  
yl]-6-methyl-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual  
stereoisomer and mixtures of stereoisomers; or the pharmaceutically acceptable  
salt thereof.

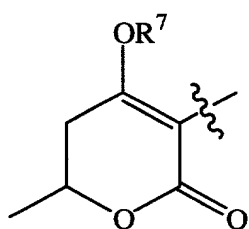
48. A compound selected from the group consisting of:

7-(2,4-dimethoxy-phenyl)-5-(4-hydroxy-6-methyl-2-oxo-2*H*-pyran-3-yl)-  
2,2-dimethyl-2,3,6,7-tetrahydro-[1,4]thiazepine-3-carboxylic acid; and

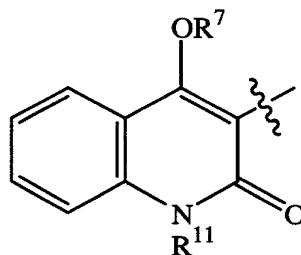
2-({ 1-[7-(2,4-dimethoxy-phenyl)-5-(4-hydroxy-6-methyl-2-oxo-  
2*H*-pyran-3-yl)-2,2-dimethyl-2,3,6,7-tetrahydro-[1,4]thiazepin-3-yl]-methanoyl }-  
amino)-propionic acid *tert*-butyl ester;

and the *N*-oxide derivatives, prodrug derivatives, protected derivatives;  
and the pharmaceutically acceptable salts thereof..

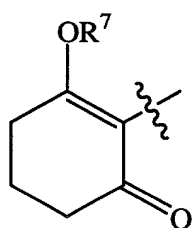
49. The compound of Claim 1 in which A<sup>1</sup> is a group selected from  
Formulae (b), (c), (d), (e) and (f):



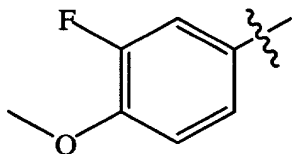
(b)



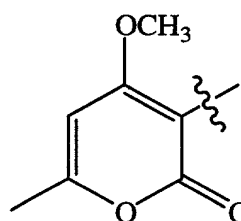
(c)



(d)



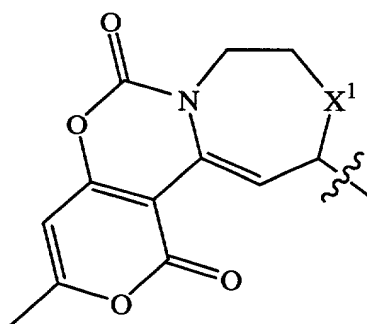
(e)



(f)

in which  $R^7$  is hydrogen or methyl,  $R^{11}$  is hydrogen or  $(C_{1-6})$ alkyl and the free valance is attached to  $A^2$ , or

$A^2$  and  $A^1$  together with  $R^1$  and the atoms to which  $A^1$  and  $R^1$  are attached forms a group of Formula (g):



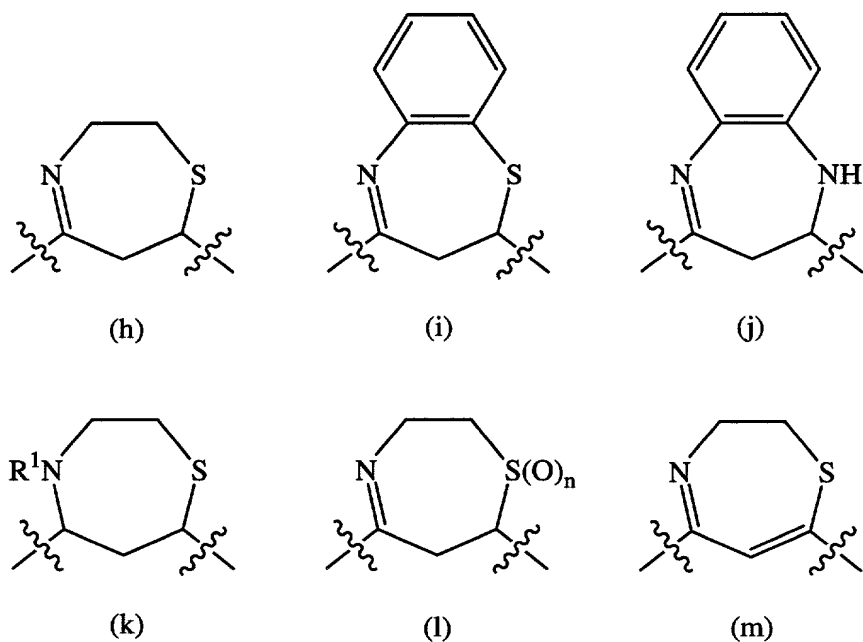
(g)

wherein  $X^1$  is -S- and the free valance is attached to  $A^3$ ; and

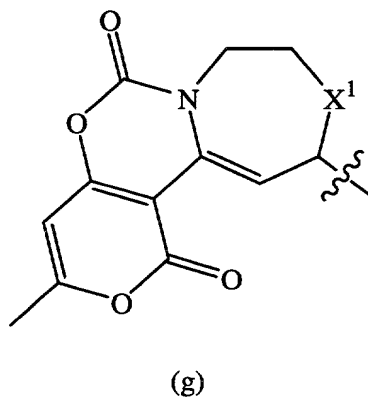
$A^2$  is as defined above or is a monocyclic or fused bicyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein  $A^2$  may be substituted with a group selected from  $-X^2R^8$ ,  $-X^2OR^8$ ,  $-X^2C(O)R^8$ ,  $-X^2OC(O)R^8$ ,

$-X^2C(O)OR^8$ ,  $-X^2SR^8$ ,  $-X^2S(O)R^8$ ,  $-X^2S(O)_2R^8$ ,  $-X^2NR^4R^8$ ,  $-X^2NR^4C(O)R^8$ ,  
 $-X^2NR^4C(O)OR^8$ ,  $-X^2C(O)NR^4R^8$ ,  $-X^2NR^4C(O)NR^4R^8$ ,  $-X^2NR^4C(NR^4)NR^4R^8$ ,  
 $-X^2NR^4S(O)_2R^8$  and  $-X^2S(O)_2NR^4R^8$ , wherein  $X^2$  is a bond or  $(C_{1-6})$ alkylene,  $R^8$   
 is  $-X^2R^9$  wherein  $X^2$  is as defined above and  $R^9$  is aryl containing a total of 6 to  
 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated,  
 partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each  
 containing a total of 3 to 10 ring atoms, and  $R^4$  at each occurrence independently  
 is hydrogen,  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-6})$ alkyl, wherein each ring within  
 $A^2$  and  $R^8$  contains from 3 to 8 ring atoms and may be substituted with 1 to 3  
 groups independently selected from  $(C_{1-6})$ alkyl, cyano, halo, nitro,  
 halo-substituted  $(C_{1-6})$ alkyl,  $-X^2OR^4$ ,  $-X^2C(O)R^6$ ,  $-X^2OC(O)R^6$ ,  $-X^2C(O)OR^4$ ,  
 $-X^2SR^4$ ,  $-X^2S(O)R^6$ ,  $-X^2S(O)_2R^6$ ,  $-X^2NR^4R^4$ ,  $-X^2NR^4C(O)R^6$ ,  $-X^2NR^4C(O)OR^4$ ,  
 $-X^2C(O)NR^4R^4$ ,  $-X^2NR^4C(O)NR^4R^4$ ,  $-X^2NR^4C(NR^4)NR^4R^4$ ,  
 $-X^2C(O)NR^4X^2C(O)OR^4$ ,  $-X^2NR^4S(O)_2R^6$  and  $-X^2S(O)_2NR^4R^4$ , wherein  $X^2$  and  
 $R^4$  are as defined above and  $R^6$  is  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-6})$ alkyl, and  
 wherein any said heteroalkylene, carbocycloalkyl and heterocycloalkyl rings  
 within  $A^2$  and  $R^8$  may be substituted further with 1 to 2 groups independently  
 selected from  $(C_{1-6})$ alkylidene, oxo, imino and thioxo, with the proviso that only  
 one of  $A^2$  and  $R^8$  is a fused polycyclic ring system; and the *N*-oxide derivatives,  
 prodrug derivatives, protected derivatives, individual stereoisomers and mixtures  
 of stereoisomers; and the pharmaceutically acceptable salts thereof.

50. The compound of Claim 49 in which  $A^2$  is a group selected from  
 Formulae (h), (i), (j), (k), (l) and (m):



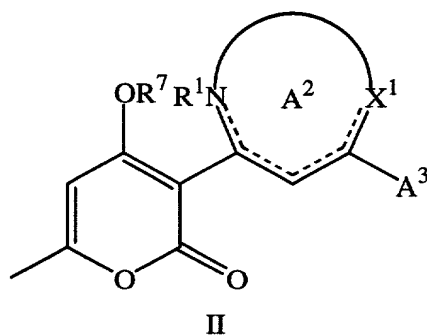
in which  $n$  is 1 or 2 and  $R^1$  is acetyl or trifluoroacetyl or  $A^2$  and  $A^1$  together with  $R^1$  and the atoms to which  $A^1$  and  $R^1$  are attached forms a group of Formula (g):



5 wherein  $X^1$  is -S- and the free valance is attached to  $A^3$ ; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

51. A compound of Formula II:





in which:

the dashed lines indicate optional unsaturation without violating valency rules;

$R^1$  is hydrogen,  $(C_{1-6})$ alkyl or  $-C(O)R^6$ , wherein  $R^6$  is as defined below, or  $R^1$  is absent when a double bond exists between the nitrogen atom to which  $R^1$  is attached and an adjacent ring atom or  $R^1$  is as defined below;

$R^7$  is hydrogen;

$X^1$  is  $-NR^2-$ ,  $-S-$ ,  $-S(O)-$ ,  $-S(O)_2-$  or  $-O-$ , wherein  $R^2$  is hydrogen or  $(C_{1-6})$ alkyl or is absent when a double bond exists between the nitrogen atom to which  $R^2$  is attached and an adjacent ring atom;

$A^2$  is a monocyclic or fused bicyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein  $A^2$  may be substituted with a group selected from  $-R^8$ ,  $-X^2OR^8$ ,  $-X^2C(O)R^8$ ,  $-X^2OC(O)R^8$ ,  $-X^2C(O)OR^8$ ,  $-X^2SR^8$ ,  $-X^2S(O)R^8$ ,  $-X^2S(O)_2R^8$ ,  $-X^2NR^4R^8$ ,  $-X^2NR^4C(O)R^8$ ,  $-X^2NR^4C(O)OR^8$ ,  $-X^2C(O)NR^4R^8$ ,  $-X^2NR^4C(O)NR^4R^8$ ,  $-X^2NR^4C(NR^4)NR^4R^8$ ,  $-X^2NR^4S(O)_2R^8$  and  $-X^2S(O)_2NR^4R^8$ , wherein  $X^2$  is a bond or  $(C_{1-6})$ alkylene,  $R^8$  is  $-X^2R^9$  wherein  $X^2$  is as defined above and  $R^9$  is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and  $R^4$  at each occurrence independently is hydrogen,  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-6})$ alkyl, wherein each ring within  $A^2$  and  $R^8$  contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from  $(C_{1-6})$ alkyl, cyano, halo, nitro, halo-substituted  $(C_{1-6})$ alkyl,  $-X^2OR^4$ ,

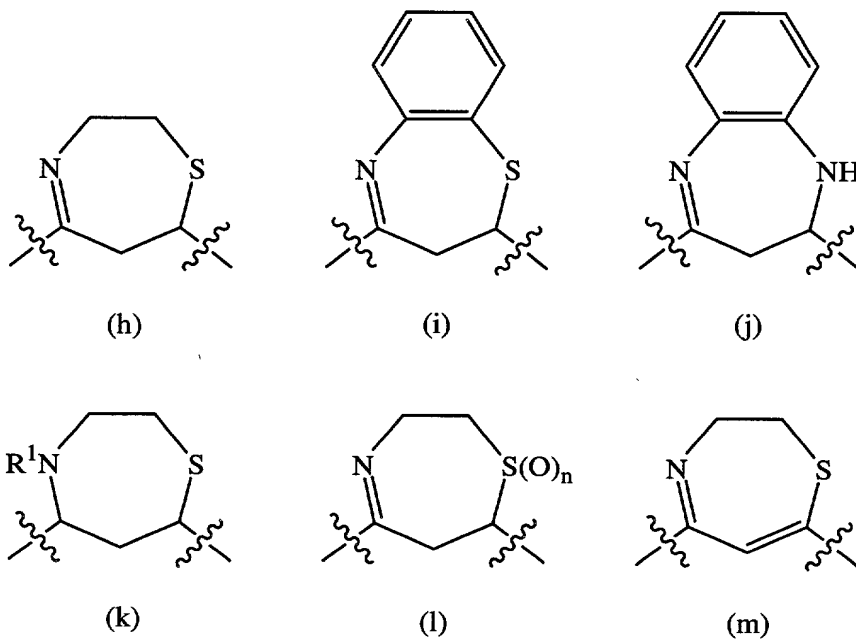
-X<sup>2</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>OC(O)R<sup>6</sup>, -X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>SR<sup>4</sup>, -X<sup>2</sup>S(O)R<sup>6</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>6</sup>,  
 -X<sup>2</sup>NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>4</sup>,  
 -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>6</sup> and  
 -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>4</sup>, wherein X<sup>2</sup> and R<sup>4</sup> are as defined above and R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or  
 halo-substituted (C<sub>1-6</sub>)alkyl, and wherein any said heteroalkylene, carbocycloalkyl  
 and heterocycloalkyl rings within A<sup>2</sup> and R<sup>8</sup> may be substituted further with 1 to  
 2 groups independently selected from (C<sub>1-6</sub>)alkylidene, oxo, imino and thioxo  
 with the proviso that only one of A<sup>2</sup> and R<sup>8</sup> is a fused polycyclic ring system; and

A<sup>3</sup> is a monocyclic or fused polycyclic ring system selected from aryl  
 containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14  
 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or  
 heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A<sup>3</sup> may  
 be substituted with a group selected from -R<sup>9</sup>, -X<sup>2</sup>OR<sup>9</sup>, -X<sup>2</sup>C(O)R<sup>9</sup>, -X<sup>2</sup>OC(O)R<sup>9</sup>,  
 -X<sup>2</sup>C(O)OR<sup>9</sup>, -X<sup>2</sup>SR<sup>9</sup>, -X<sup>2</sup>S(O)R<sup>9</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>9</sup>,  
 -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>9</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>9</sup>,  
 -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>9</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>9</sup>, wherein X<sup>2</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>9</sup>  
 is -X<sup>2</sup>R<sup>10</sup> wherein X<sup>2</sup> is as defined above and R<sup>10</sup> is aryl containing a total of 6 to  
 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated,  
 partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each  
 containing a total of 3 to 10 ring atoms, and R<sup>4</sup> at each occurrence independently  
 is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, wherein each ring within  
 A<sup>3</sup> and R<sup>10</sup> contains from 3 to 8 ring atoms and may be substituted with 1 to 3  
 groups independently selected from (C<sub>1-6</sub>)alkyl, cyano, halo, nitro,  
 halo-substituted (C<sub>1-6</sub>)alkyl, -X<sup>2</sup>OR<sup>4</sup>, -X<sup>2</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>OC(O)R<sup>6</sup>, -X<sup>2</sup>C(O)OR<sup>4</sup>,  
 -X<sup>2</sup>SR<sup>4</sup>, -X<sup>2</sup>S(O)R<sup>6</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>4</sup>,  
 -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>6</sup> and  
 -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>4</sup>, wherein X<sup>2</sup> and R<sup>4</sup> are as defined above and R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or  
 halo-substituted (C<sub>1-6</sub>)alkyl, and wherein any said carbocycloalkyl and  
 heterocycloalkyl rings within A<sup>3</sup> and R<sup>10</sup> may be substituted further with 1 to 2  
 groups independently selected from (C<sub>1-6</sub>)alkylidene, oxo, imino and thioxo with

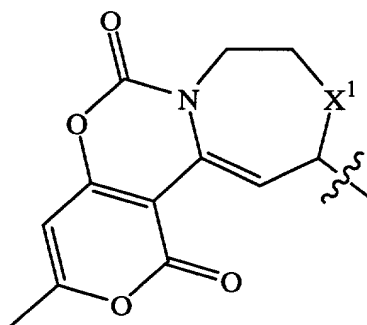
the proviso that only one of  $A^3$  and  $R^{10}$  is a fused polycyclic ring system; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof;

provided, however, Formula II does not represent a compound wherein  $A^2$  is 2,3,6,7-tetrahydro-[1,4]thiazepinylen, 2,3-dihydro-benzo[*b*][1,4]thiazepinylen or 7-trifluoro-2,3-dihydro-benzo[*b*][1,4]thiazepinylen and  $A^3$  is benzo[1,3]dioxolyl, indolyl, phenyl, pyridyl or thienyl, wherein said phenyl may be substituted with 1 to 3 groups independently selected from halo, nitro, hydroxy,  $(C_{1-4})$ alkyl,  $(C_{1-4})$ alkylsulfanyl and  $(C_{1-4})$ alkyloxy or any *N*-oxide derivative; protected derivative, individual stereoisomer or mixture of stereoisomers, or pharmaceutically acceptable salt thereof.

52. The compound of Claim 51 in which  $A^2$  is a group selected from Formulae (h), (i), (j), (k), (l) and (m):



in which  $n$  is 1 or 2 and  $R^1$  is acetyl or trifluoroacetyl or  $A^2$  and  $A^1$  together with  $R^1$  and the atoms to which  $A^1$  and  $R^1$  are attached forms a group of Formula (g):



(g)

wherein  $X^1$  is -S- and the free valance is attached to  $A^3$ ; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

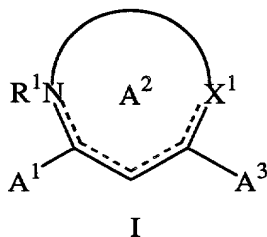
53. The compound of Claim 52 in which  $A^3$  is phenyl or heteroaryl containing a total of 5 to 9 ring atoms, wherein  $A^3$  may be substituted with a group selected from  $-R^9$ ,  $-X^2OR^9$ ,  $-X^2SR^9$  and  $-X^2S(O)_2R^9$ , wherein  $R^9$  is  $-X^2R^{10}$ ,  $X^2$  is a bond or  $(C_{1-6})$ alkylene and  $R^{10}$  is phenyl or heteroaryl containing a total of 5 to 6 ring atoms, wherein each ring within  $A^3$  and  $R^{10}$  may be substituted with 1 to 3 groups independently selected from  $(C_{1-6})$ alkyl, halo, halo-substituted  $(C_{1-6})$ alkyl,  $-X^2OR^4$ ,  $-X^2SR^4$ ,  $-X^2S(O)_2R^4$  and  $-X^2NR^4R^4$ , wherein  $R^4$  at each occurrence independently is hydrogen,  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-6})$ alkyl and  $R^6$  is  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-6})$ alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

54. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1, 47 or 51 or a *N*-oxide derivative, prodrug derivative, individual isomer or mixture of isomers or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable excipient.

55. The pharmaceutical composition of Claim 54, further comprising at least one known cancer chemotherapeutic agent.

56. The pharmaceutical composition of Claim 55, wherein said cancer therapeutic agent is selected from the group consisting of busulfan, cis-platin, mitomycin C, carboplatin, colchicine, vinblastine, paclitaxel, docetaxel, camptothecin, topotecan, doxorubicin, etoposide, 5-azacytidine, 5-fluorouracil, methotrexate, 5-fluoro-2'-deoxy-uridine, ara-C, hydroxyurea, thioguanine, melphalan, chlorambucil, cyclophosphamide, ifosfamide, vincristine, mitoguanzone, epirubicin, aclarubicin, bleomycin, imitoxantrone, elliptinium, fludarabine, octreotide, retinoic acid, tamoxifen, Herceptin®, Rituxan® and alanosine.

57. A method of treating a disorder responsive to the induction of apoptosis in an animal suffering said disorder, comprising administering to a mammal in need of such treatment an effective amount of a compound of Formula I:



in which:

the dashed lines indicate optional unsaturation without violating valency rules;

R¹ is hydrogen, (C<sub>1-6</sub>)alkyl or -C(O)R⁶, wherein R⁶ is as defined below, or R¹ is absent when a double bond exists between the nitrogen atom to which R¹ is attached and an adjacent ring atom or R¹ is as defined below;

X¹ is -NR²-, -S-, -S(O)-, -S(O)<sub>2</sub>- or -O-, wherein R² is hydrogen or (C<sub>1-6</sub>)alkyl or is absent when a double bond exists between the nitrogen atom to which R² is attached and an adjacent ring atom;

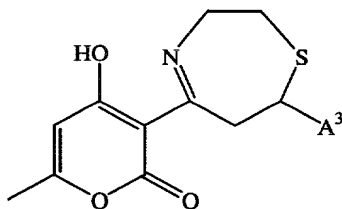
$A^1$  is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, or  $A^1$  together with  $R^1$  and the atoms to which  $A^1$  and  $R^1$  are attached forms a fused polycyclic ring system selected from heteroaryl and unsaturated, partially unsaturated or saturated heterocycloalkyl in any case containing a total of 10 to 15 ring atoms, wherein  $A^1$  may be substituted with a group selected from  $-R^3$ ,  $-X^2OR^3$ ,  $-X^2C(O)R^3$ ,  $-X^2OC(O)R^3$ ,  $-X^2C(O)OR^3$ ,  $-X^2SR^3$ ,  $-X^2S(O)R^3$ ,  $-X^2S(O)_2R^3$ ,  $-X^2NR^3R^4$ ,  $-X^2NR^4C(O)R^3$ ,  $-X^2NR^4C(O)OR^3$ ,  $-X^2C(O)NR^3R^4$ ,  $-X^2NR^4C(O)NR^3R^4$ ,  $-X^2NR^4C(NR^4)NR^3R^4$ ,  $-X^2NR^4S(O)_2R^3$  and  $-X^2S(O)_2NR^3R^4$ , wherein  $X^2$  is a bond or  $(C_{1-6})$ alkylene,  $R^3$  is  $-X^2R^5$  wherein  $X^2$  is as defined above and  $R^5$  is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and  $R^4$  at each occurrence independently is hydrogen,  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-6})$ alkyl, wherein each ring within  $A^1$  and  $R^5$  contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from  $(C_{1-6})$ alkyl, cyano, halo, nitro, halo-substituted  $(C_{1-6})$ alkyl,  $-X^2OR^4$ ,  $-X^2C(O)R^6$ ,  $-X^2OC(O)R^6$ ,  $-X^2C(O)OR^4$ ,  $-X^2SR^4$ ,  $-X^2S(O)R^6$ ,  $-X^2S(O)_2R^6$ ,  $-X^2NR^4R^4$ ,  $-X^2NR^4C(O)R^6$ ,  $-X^2NR^4C(O)OR^4$ ,  $-X^2C(O)NR^4R^4$ ,  $-X^2NR^4C(O)NR^4R^4$ ,  $-X^2NR^4C(NR^4)NR^4R^4$ ,  $-X^2NR^4S(O)_2R^6$  and  $-X^2S(O)_2NR^4R^4$ , wherein  $X^2$  and  $R^4$  are as defined above and  $R^6$  is  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-6})$ alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within  $A^1$  and  $R^5$  may be substituted further with 1 to 2 groups independently selected from  $(C_{1-6})$ alkylidene, oxo, imino and thioxo, with the provisos that only one of  $A^1$  and  $R^5$  is a fused polycyclic ring system;

$A^2$  is a monocyclic or fused bicyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein  $A^2$  may be substituted with a group selected

from  $-R^8$ ,  $-X^2OR^8$ ,  $-X^2C(O)R^8$ ,  $-X^2OC(O)R^8$ ,  $-X^2C(O)OR^8$ ,  $-X^2SR^8$ ,  $-X^2S(O)R^8$ ,  
 $-X^2S(O)_2R^8$ ,  $-X^2NR^4R^8$ ,  $-X^2NR^4C(O)R^8$ ,  $-X^2NR^4C(O)OR^8$ ,  $-X^2C(O)NR^4R^8$ ,  
 $-X^2NR^4C(O)NR^4R^8$ ,  $-X^2NR^4C(NR^4)NR^4R^8$ ,  $-X^2NR^4S(O)_2R^8$  and  $-X^2S(O)_2NR^4R^8$ ,  
wherein  $X^2$  is a bond or  $(C_{1-6})$ alkylene,  $R^8$  is  $-X^2R^9$  wherein  $X^2$  is as defined above  
and  $R^9$  is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a  
total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated  
carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms,  
and  $R^4$  at each occurrence independently is hydrogen,  $(C_{1-6})$ alkyl or  
halo-substituted  $(C_{1-6})$ alkyl, wherein each ring within  $A^2$  and  $R^8$  contains from 3  
to 8 ring atoms and may be substituted with 1 to 3 groups independently selected  
from  $(C_{1-6})$ alkyl, cyano, halo, nitro, halo-substituted  $(C_{1-6})$ alkyl,  $-X^2OR^4$ ,  
 $-X^2C(O)R^6$ ,  $-X^2OC(O)R^6$ ,  $-X^2C(O)OR^4$ ,  $-X^2SR^4$ ,  $-X^2S(O)R^6$ ,  $-X^2S(O)_2R^6$ ,  
 $-X^2NR^4R^4$ ,  $-X^2NR^4C(O)R^6$ ,  $-X^2NR^4C(O)OR^4$ ,  $-X^2C(O)NR^4R^4$ ,  
 $-X^2NR^4C(O)NR^4R^4$ ,  $-X^2NR^4C(NR^4)NR^4R^4$ ,  $-X^2C(O)NR^4X^2C(O)OR^4$ ,  
 $-X^2NR^4S(O)_2R^6$  and  $-X^2S(O)_2NR^4R^4$ , wherein  $X^2$  and  $R^4$  are as defined above and  
 $R^6$  is  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-6})$ alkyl, and wherein any said  
heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within  $A^2$  and  $R^8$   
may be substituted further with 1 to 2 groups independently selected from  
 $(C_{1-6})$ alkylidene, oxo, imino and thioxo, with the proviso that only one of  $A^2$  and  
 $R^8$  is a fused polycyclic ring system; and

$A^3$  is a monocyclic or fused polycyclic ring system selected from aryl  
containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14  
ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or  
heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein  $A^3$  may  
be substituted with a group selected from  $-R^9$ ,  $-X^2OR^9$ ,  $-X^2C(O)R^9$ ,  $-X^2OC(O)R^9$ ,  
 $-X^2C(O)OR^9$ ,  $-X^2SR^9$ ,  $-X^2S(O)R^9$ ,  $-X^2S(O)_2R^9$ ,  $-X^2NR^4R^9$ ,  $-X^2NR^4C(O)R^9$ ,  
 $-X^2NR^4C(O)OR^9$ ,  $-X^2C(O)NR^4R^9$ ,  $-X^2NR^4C(O)NR^4R^9$ ,  $-X^2NR^4C(NR^4)NR^4R^9$ ,  
 $-X^2NR^4S(O)_2R^9$  and  $-X^2S(O)_2NR^4R^9$ , wherein  $X^2$  is a bond or  $(C_{1-6})$ alkylene,  $R^9$   
is  $-X^2R^{10}$  wherein  $X^2$  is as defined above and  $R^{10}$  is aryl containing a total of 6 to  
10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated,

partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R<sup>4</sup> at each occurrence independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, wherein each ring within A<sup>3</sup> and R<sup>10</sup> contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C<sub>1-6</sub>)alkyl, cyano, halo, nitro, halo-substituted (C<sub>1-6</sub>)alkyl, -X<sup>2</sup>OR<sup>4</sup>, -X<sup>2</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>OC(O)R<sup>6</sup>, -X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>SR<sup>4</sup>, -X<sup>2</sup>S(O)R<sup>6</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>6</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>4</sup>, wherein X<sup>2</sup> and R<sup>4</sup> are as defined above and R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A<sup>3</sup> and R<sup>10</sup> may be substituted further with 1 to 2 groups independently selected from (C<sub>1-6</sub>)alkylidene, oxo, imino and thioxo, with the proviso that only one of A<sup>3</sup> and R<sup>10</sup> is a fused polycyclic ring system; or an *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers, or a pharmaceutically acceptable salt thereof; with the proviso that when said compound is of Formula II(a):



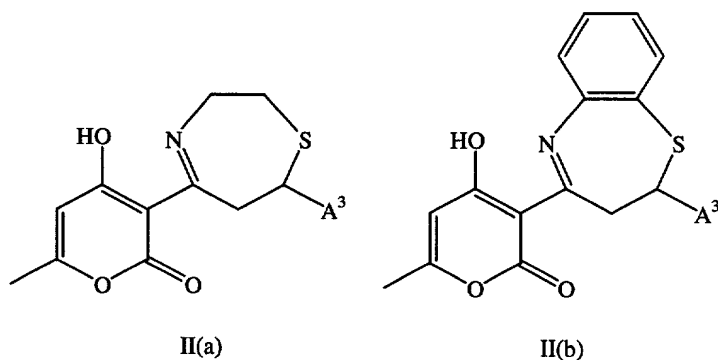
II(a)

then A<sup>3</sup> is other than:

- (a) benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, hydroxy, methyl or isopropyl; and
- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino.

58. The method of claim 57, with the further proviso that when said compound is selected from the group consisting of Formula II(a) and II(b):

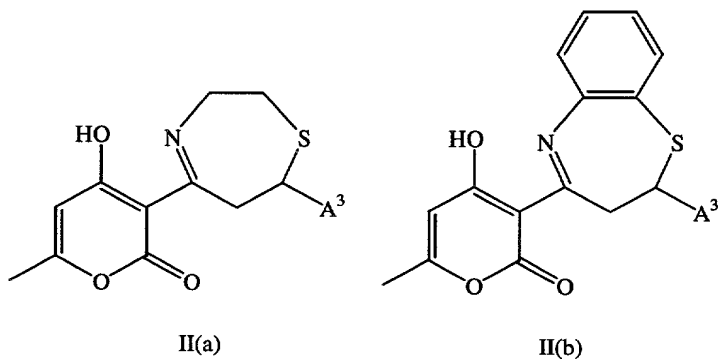




then A<sup>3</sup> is other than:

- (a) benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, nitro, hydroxy, methyl, or isopropyl; and
- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino.

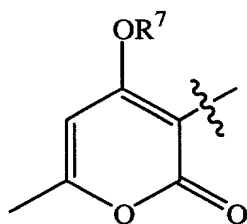
59. The method of claim 57, with the further proviso that when said compound is selected from the group consisting of Formula II(a) and II(b):



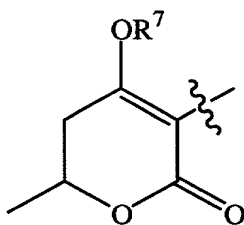
then A<sup>3</sup> is other than:

- (a) benzo[1,3]dioxolyl;
- (b) 2,3-dihydro-benzo[1,4]dioxinyl; and
- (c) phenyl which is substituted by at least one of bromo, chloro, hydroxy, nitro, methoxy and (C<sub>1-3</sub>)alkyl.

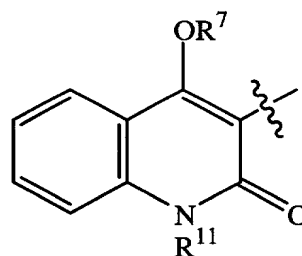
60. The method of Claim 57, wherein  $A^1$  of said compound is a group selected from Formulae (a), (b), (c), (d) and (e):



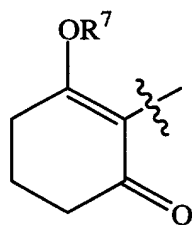
(a)



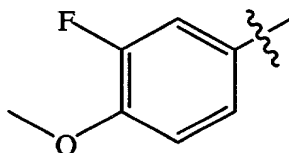
(b)



(c)



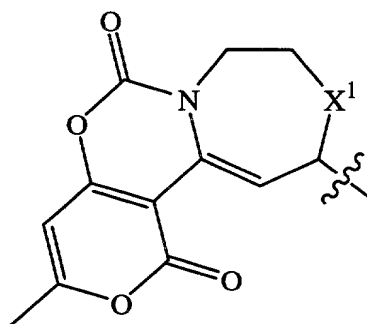
(d)



(e)

in which  $R^7$  is hydrogen or methyl,  $R^{11}$  is hydrogen or  $(C_{1-6})$ alkyl and the free valance is attached to  $A^2$ , or

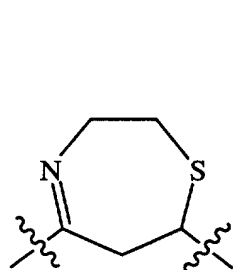
$A^2$  and  $A^1$  together with  $R^1$  and the atoms to which  $A^1$  and  $R^1$  are attached forms a group of Formula (g):



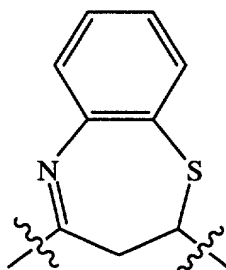
(g)

wherein  $X^1$  is -S- and the free valance is attached to  $A^3$ ; and

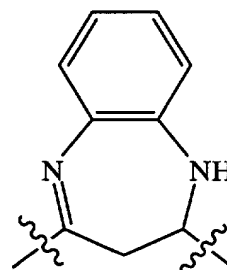
$A^2$  of said compound is as defined above or is a group selected from Formulae (h), (i), (j), (k), (l) and (m):



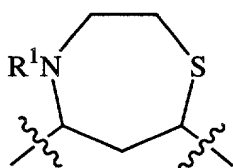
(h)



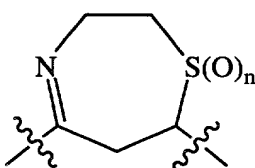
(i)



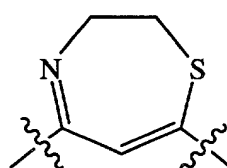
(j)



(k)



(l)



(m)

in which  $n$  is 1 or 2 and  $R^1$  is acetyl or trifluoroacetyl; or an *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers, or a pharmaceutically acceptable salt thereof.

61. The method of Claim 60, wherein  $A^3$  of said compound is phenyl or heteroaryl containing a total of 5 to 9 ring atoms, wherein  $A^3$  may be substituted with a group selected from  $-R^9$ ,  $-X^2OR^9$ ,  $-X^2SR^9$  and  $-X^2S(O)_2R^9$ , wherein  $R^9$  is  $-X^2R^{10}$ ,  $X^2$  is a bond or  $(C_{1-6})$ alkylene and  $R^{10}$  is phenyl or heteroaryl containing a total of 5 to 6 ring atoms, wherein each ring within  $A^3$  and  $R^{10}$  may be substituted with 1 to 3 groups independently selected from  $(C_{1-6})$ alkyl, halo, halo-substituted  $(C_{1-6})$ alkyl,  $-X^2OR^4$ ,  $-X^2SR^4$ ,  $-X^2S(O)_2R^6$  and  $-X^2NR^4R^4$ , wherein  $R^4$  at each occurrence independently is hydrogen,  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-6})$ alkyl and  $R^6$  is  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-6})$ alkyl; and the *N*-oxide derivatives, prodrug derivatives, protected derivatives, individual stereoisomers and mixtures of stereoisomers; and the pharmaceutically acceptable salts thereof.

62. The method of Claim 61, wherein said compound is selected from the group consisting of:

2-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

4-hydroxy-3-[7-(4-methanesulfonyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

3-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

2-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

3-hydroxy-2-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-cyclohex-2-enone;

3-hydroxy-2-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone;

4-hydroxy-6-methyl-3-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-5,6-dihydro-pyran-2-one; and

4-hydroxy-6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-5,6-dihydro-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

63. The method of claim 57, wherein said compound is selected from the list consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfonyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[4-acetyl-7-(2,4-dimethoxy-phenyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-4-(2,2,2-trifluoro-ethanoyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

5 1-[7-(2,4-dimethoxy-phenyl)-5-(3-fluoro-4-methoxyphenyl)-[1,4]thiazepan-4-yl]-ethanone;

4-hydroxy-6-methyl-3-[7-(3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

10 3-[7-(5-ethyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3[7-(2-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

15 4-hydroxy-6-methyl-3[7-(3-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(4-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

20 4-hydroxy-6-methyl-3-[7-[3-(3-trifluoromethyl-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-[3-(3,4-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-[3-(3,5-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

25 4-hydroxy-6-methyl-3-{7-[5-(3-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-{7-[5-(2-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

30 3-{7-[5-(3-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(4-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(2-chloro-5-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

5 3-[7-(4-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

10 3-[7-(1-benzenesulfonyl-1*H*-pyrrol-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(3-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

15 4-hydroxy-6-methyl-3-[7-(1-methyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3-chloro-2-methyl-5-trifluoromethyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

20 3-{7-[1-(2,4-difluoro-benzenesulfonyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-(7-[2,2']bithienyl-5-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(3,5-dichloro-phenyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

25 3-{7-[1-(4-chloro-phenyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-chloro-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

30 4-hydroxy-6-methyl-3-[7-(6-*p*-tolylsulfanyl-imidazo[2,1-*b*]thiazol-5-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(4,5-dibromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2-chloro-5-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

5 3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methylsulfanyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

10 3-[7-(5-chloro-1-methyl-3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[4-(2,4-dimethoxy-phenyl)-4,5-dihydro-3*H*-benzo[*b*][1,4]diazepin-2-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

15 3-[7-2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-1*H*-quinolin-2-one;

4-hydroxy-6-methyl-3-[7-(4-trifluoromethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

20 3-[7-(bis-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-hydroxy-2-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone;

25 3-[7-(2,4-dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1*H*-1λ<sup>4</sup>-[1,4]thiazepin-5-yl]-4-hydroxy-6-methoxy-pyran-2-one;

10-(2,4-dimethoxy-phenyl)-3-methyl-7,8-dihydro-10*H*-2,5-dioxa-9-thia-6a-aza-cyclohepta[*a*]naphthalene-1,6-dione;

30 3-[7-(2,4-dimethoxy-phenyl)-1,1-dioxo-2,3,6,7-tetrahydro-1*H*-1λ<sup>6</sup>-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

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3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-(7-[2,2']bithienyl-5-yl-2,3-dihydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

2-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone; and

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

64. A method of treating a disorder responsive to the induction of apoptosis in an animal suffering said disorder, comprising administering to a mammal in need of such treatment an effective amount of a compound selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfonyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(4-ethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(3-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

3-[7-(2-bromo-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,3-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;



6-methyl-3-(2-*p*-tolyl-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl)-pyran-2-one;

4-hydroxy-6-methyl-3-[2-(4-methylsulfanyl-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-pyran-2-one; and

3-[7-(2,4-dimethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-3-[7-(4-chloro-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; and

4-hydroxy-3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

65. The method of claim 64, wherein said compound is selected from the group consisting of:

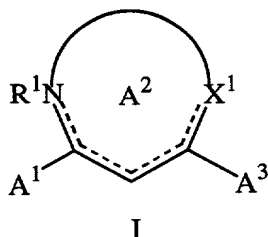
4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; and

6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

66. A method for treating or preventing cancer, comprising administering to an animal in need of such treatment an effective amount of a compound of Formula I:



in which:

the dashed lines indicate optional unsaturation without violating valency rules;

$R^1$  is hydrogen,  $(C_{1-6})$ alkyl or  $-C(O)R^6$ , wherein  $R^6$  is as defined below, or  $R^1$  is absent when a double bond exists between the nitrogen atom to which  $R^1$  is attached and an adjacent ring atom or  $R^1$  is as defined below;

$X^1$  is  $-NR^2-$ ,  $-S-$ ,  $-S(O)-$ ,  $-S(O)_2-$  or  $-O-$ , wherein  $R^2$  is hydrogen or  $(C_{1-6})$ alkyl or is absent when a double bond exists between the nitrogen atom to which  $R^2$  is attached and an adjacent ring atom;

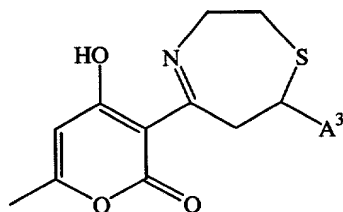
$A^1$  is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, or  $A^1$  together with  $R^1$  and the atoms to which  $A^1$  and  $R^1$  are attached forms a fused polycyclic ring system selected from heteroaryl and unsaturated, partially unsaturated or saturated heterocycloalkyl in any case containing a total of 10 to 15 ring atoms, wherein  $A^1$  may be substituted with a group selected from  $-R^3$ ,  $-X^2OR^3$ ,  $-X^2C(O)R^3$ ,  $-X^2OC(O)R^3$ ,  $-X^2C(O)OR^3$ ,  $-X^2SR^3$ ,  $-X^2S(O)R^3$ ,  $-X^2S(O)_2R^3$ ,  $-X^2NR^3R^4$ ,  $-X^2NR^4C(O)R^3$ ,  $-X^2NR^4C(O)OR^3$ ,  $-X^2C(O)NR^3R^4$ ,  $-X^2NR^4C(O)NR^3R^4$ ,  $-X^2NR^4C(NR^4)NR^3R^4$ ,  $-X^2NR^4S(O)_2R^3$  and  $-X^2S(O)_2NR^3R^4$ , wherein  $X^2$  is a bond or  $(C_{1-6})$ alkylene,  $R^3$  is  $-X^2R^5$  wherein  $X^2$  is as defined above and  $R^5$  is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and  $R^4$  at each occurrence independently is hydrogen,  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-6})$ alkyl, wherein each ring within  $A^1$  and  $R^5$  contains from 3 to 8 ring atoms and may be

substituted with 1 to 3 groups independently selected from (C<sub>1-6</sub>)alkyl, cyano, halo, nitro, halo-substituted (C<sub>1-6</sub>)alkyl, -X<sup>2</sup>OR<sup>4</sup>, -X<sup>2</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>OC(O)R<sup>6</sup>, -X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>SR<sup>4</sup>, -X<sup>2</sup>S(O)R<sup>6</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>6</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>4</sup>, wherein X<sup>2</sup> and R<sup>4</sup> are as defined above and R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A<sup>1</sup> and R<sup>5</sup> may be substituted further with 1 to 2 groups independently selected from (C<sub>1-6</sub>)alkylidene, oxo, imino and thioxo, with the provisos that only one of A<sup>1</sup> and R<sup>5</sup> is a fused polycyclic ring system;

A<sup>2</sup> is a monocyclic or fused bicyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein A<sup>2</sup> may be substituted with a group selected from -R<sup>8</sup>, -X<sup>2</sup>OR<sup>8</sup>, -X<sup>2</sup>C(O)R<sup>8</sup>, -X<sup>2</sup>OC(O)R<sup>8</sup>, -X<sup>2</sup>C(O)OR<sup>8</sup>, -X<sup>2</sup>SR<sup>8</sup>, -X<sup>2</sup>S(O)R<sup>8</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>8</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>8</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>8</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>8</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>8</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>8</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>8</sup>, -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>8</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>8</sup>, wherein X<sup>2</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>8</sup> is -X<sup>2</sup>R<sup>9</sup> wherein X<sup>2</sup> is as defined above and R<sup>9</sup> is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R<sup>4</sup> at each occurrence independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, wherein each ring within A<sup>2</sup> and R<sup>8</sup> contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C<sub>1-6</sub>)alkyl, cyano, halo, nitro, halo-substituted (C<sub>1-6</sub>)alkyl, -X<sup>2</sup>OR<sup>4</sup>, -X<sup>2</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>OC(O)R<sup>6</sup>, -X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>SR<sup>4</sup>, -X<sup>2</sup>S(O)R<sup>6</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>6</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>4</sup>, wherein X<sup>2</sup> and R<sup>4</sup> are as defined above and R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, and wherein any said heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within A<sup>2</sup> and R<sup>8</sup> may be substituted further with 1 to 2 groups independently selected from

(C<sub>1-6</sub>)alkylidene, oxo, imino and thioxo, with the proviso that only one of A<sup>2</sup> and R<sup>8</sup> is a fused polycyclic ring system; and

A<sup>3</sup> is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A<sup>3</sup> may be substituted with a group selected from -R<sup>9</sup>, -X<sup>2</sup>OR<sup>9</sup>, -X<sup>2</sup>C(O)R<sup>9</sup>, -X<sup>2</sup>OC(O)R<sup>9</sup>, -X<sup>2</sup>C(O)OR<sup>9</sup>, -X<sup>2</sup>SR<sup>9</sup>, -X<sup>2</sup>S(O)R<sup>9</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>9</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>9</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>9</sup>, wherein X<sup>2</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>9</sup> is -X<sup>2</sup>R<sup>10</sup> wherein X<sup>2</sup> is as defined above and R<sup>10</sup> is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R<sup>4</sup> at each occurrence independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, wherein each ring within A<sup>3</sup> and R<sup>10</sup> contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C<sub>1-6</sub>)alkyl, cyano, halo, nitro, halo-substituted (C<sub>1-6</sub>)alkyl, -X<sup>2</sup>OR<sup>4</sup>, -X<sup>2</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>OC(O)R<sup>6</sup>, -X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>SR<sup>4</sup>, -X<sup>2</sup>S(O)R<sup>6</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>6</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>4</sup>, wherein X<sup>2</sup> and R<sup>4</sup> are as defined above and R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A<sup>3</sup> and R<sup>10</sup> may be substituted further with 1 to 2 groups independently selected from (C<sub>1-6</sub>)alkylidene, oxo, imino and thioxo, with the proviso that only one of A<sup>3</sup> and R<sup>10</sup> is a fused polycyclic ring system; or an N-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers, or a pharmaceutically acceptable salt thereof; with the proviso that when said compound is of Formula II(a):

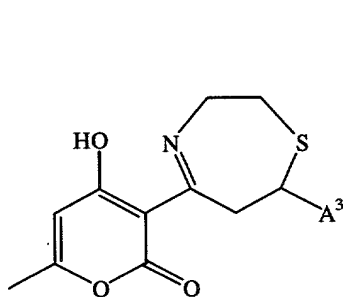


II(a)

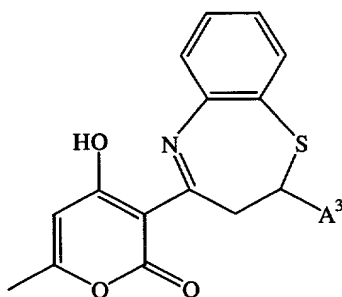
then A<sup>3</sup> is other than:

- (a) benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, hydroxy, methyl or isopropyl; and
- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

67. The method of claim 66, with the further proviso that when said compound is selected the group consisting of Formula II(a) and II(b):



II(a)



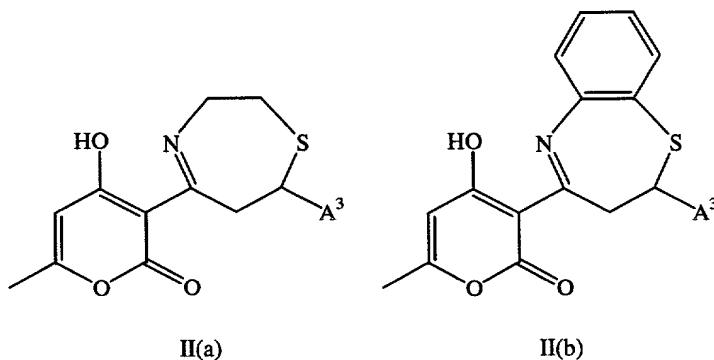
II(b)

then A<sup>3</sup> is other than:

- (a) benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, nitro, hydroxy, methyl, or isopropyl; and
- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

68. The method of claim 66, with the further proviso that when said compound is selected the group consisting of Formula II(a) and II(b):

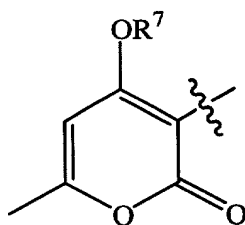


then  $A^3$  is other than:

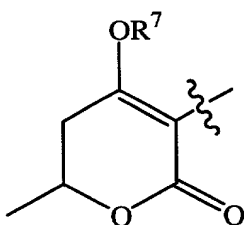
- (a) benzo[1,3]dioxolyl;
- (b) 2,3-dihydro-benzo[1,4]dioxinyl; and
- (c) phenyl which is substituted by at least one of bromo, chloro, hydroxy, nitro, methoxy and  $(C_{1-3})$ alkyl; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof..

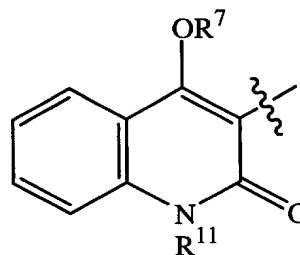
69. The method of Claim 66, wherein  $A^1$  of said compound is a group selected from Formulae (a), (b), (c), (d) and (e):



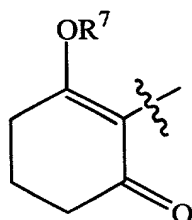
(a)



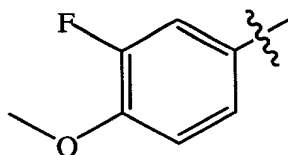
(b)



(c)



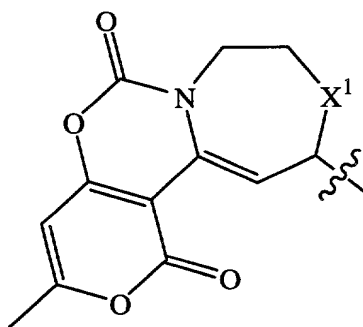
(d)



(e)

in which  $R^7$  is hydrogen or methyl,  $R^{11}$  is hydrogen or  $(C_{1-6})$ alkyl and the free valance is attached to  $A^2$ , or

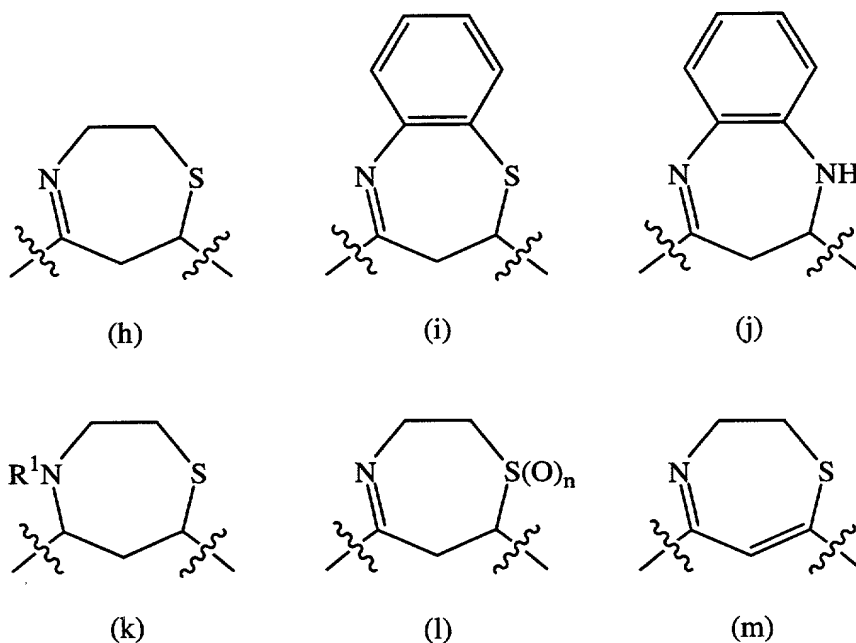
$A^2$  and  $A^1$  together with  $R^1$  and the atoms to which  $A^1$  and  $R^1$  are attached forms a group of Formula (g):



(g)

wherein  $X^1$  is -S- and the free valance is attached to  $A^3$ ; and

$A^2$  of said compound is as defined above or is a group selected from Formulae (h), (i), (j), (k), (l) and (m):



in which n is 1 or 2 and R<sup>1</sup> is acetyl or trifluoroacetyl; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

70. The method of Claim 69, wherein A<sup>3</sup> of said compound is phenyl or heteroaryl containing a total of 5 to 9 ring atoms, wherein A<sup>3</sup> may be substituted with a group selected from -R<sup>9</sup>, -X<sup>2</sup>OR<sup>9</sup>, -X<sup>2</sup>SR<sup>9</sup> and -X<sup>2</sup>S(O)<sub>2</sub>R<sup>9</sup>, wherein R<sup>9</sup> is -X<sup>2</sup>R<sup>10</sup>, X<sup>2</sup> is a bond or (C<sub>1-6</sub>)alkylene and R<sup>10</sup> is phenyl or heteroaryl containing a total of 5 to 6 ring atoms, wherein each ring within A<sup>3</sup> and R<sup>10</sup> may be substituted with 1 to 3 groups independently selected from (C<sub>1-6</sub>)alkyl, halo, halo-substituted (C<sub>1-6</sub>)alkyl, -X<sup>2</sup>OR<sup>4</sup>, -X<sup>2</sup>SR<sup>4</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>6</sup> and -X<sup>2</sup>NR<sup>4</sup>R<sup>4</sup>, wherein R<sup>4</sup> at each occurrence independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl and R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

71. The method of Claim 70, wherein said compound is selected from the group consisting of:



4-hydroxy-3-[7-(2-methoxy-4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

2-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

4-hydroxy-3-[7-(4-methanesulfonyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

3-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

2-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

3-hydroxy-2-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-cyclohex-2-enone;

3-hydroxy-2-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone;

4-hydroxy-6-methyl-3-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-5,6-dihydro-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-5,6-dihydro-pyran-2-one; and

3-[7-(2,4-dimethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

72. The method of claim 66, wherein said compound is selected from the list consisting of:

3-[4-acetyl-7-(2,4-dimethoxy-phenyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-4-(2,2,2-trifluoro-ethanoyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

5 1-[7-(2,4-dimethoxy-phenyl)-5-(3-fluoro-4-methoxyphenyl)-[1,4]thiazepan-4-yl]-ethanone;

4-hydroxy-6-methyl-3-[7-(3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-ethyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3[7-(2-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(3-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(4-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-[3-(3-trifluoromethyl-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-[3-(3,4-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-[3-(3,5-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(3-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-{7-[5-(2-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(3-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(4-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(2-chloro-5-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

5 3-[7-(4-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(1-benzenesulfonyl-1*H*-pyrrol-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(3-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(1-methyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3-chloro-2-methyl-5-trifluoromethyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(2,4-difluoro-benzenesulfonyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-(7-[2,2']bithienyl-5-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(3,5-dichloro-phenyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(4-chloro-phenyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-chloro-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(6-*p*-tolylsulfanyl-imidazo[2,1-*b*]thiazol-5-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(4,5-dibromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2-chloro-5-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

5 3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methylsulfanyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

10 3-[7-(5-chloro-1-methyl-3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[4-(2,4-dimethoxy-phenyl)-4,5-dihydro-3*H*-benzo[*b*][1,4]diazepin-2-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

15 3-[7-2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-1*H*-quinolin-2-one;

4-hydroxy-6-methyl-3-[7-(4-trifluoromethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

20 3-[7-(bis-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-hydroxy-2-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone;

25 3-[7-(2,4-dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1*H*-1λ<sup>4</sup>-[1,4]thiazepin-5-yl]-4-hydroxy-6-methoxy-pyran-2-one;

10-(2,4-dimethoxy-phenyl)-3-methyl-7,8-dihydro-10*H*-2,5-dioxa-9-thia-6a-aza-cyclohepta[*a*]naphthalene-1,6-dione;

30 3-[7-(2,4-dimethoxy-phenyl)-1,1-dioxo-2,3,6,7-tetrahydro-1*H*-1λ<sup>6</sup>-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-(7-[2,2']bithienyl-5-yl)-2,3-dihydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

2-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone; and

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

73. A method for treating or preventing cancer, comprising administering to an animal in need of such treatment an effective amount of a compound selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(4-ethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(3-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

3-[7-(2-bromo-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,3-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

6-methyl-3-(2-*p*-tolyl-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl)-pyran-2-one;

4-hydroxy-6-methyl-3-[2-(4-methylsulfanyl-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-pyran-2-one;

4-hydroxy-3-[7-(4-chloro-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; and

4-hydroxy-3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

74. The method of claim 73, wherein said compound is selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; and

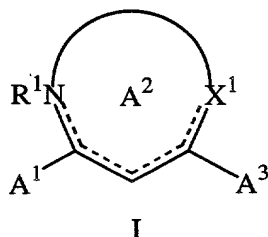
6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

75. The method of Claims 66 and 73, wherein said cancer is selected from the group consisting of Hodgkin's disease, non-Hodgkin's lymphoma, acute and chronic lymphocytic leukemias, multiple myeloma, neuroblastoma, breast carcinoma, ovarian carcinoma, lung carcinoma, Wilms' tumor, cervical carcinoma, testicular carcinoma, soft-tissue sarcoma, chronic lymphocytic leukemia, primary macroglobulinemia, bladder carcinoma, chronic granulocytic leukemia, primary brain carcinoma, malignant melanoma, small-cell lung carcinoma, stomach carcinoma, colon carcinoma, malignant pancreatic insulinoma, malignant carcinoid carcinoma, choriocarcinoma, mycosis fungoides,

head and neck carcinoma, osteogenic sarcoma, pancreatic carcinoma, acute granulocytic leukemia, hairy cell leukemia, neuroblastoma, rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinoma, thyroid carcinoma, esophageal carcinoma, malignant hypercalcemia, cervical hyperplasia, renal cell carcinoma, endometrial carcinoma, polycythemia vera, essential thrombocytosis, adrenal cortex carcinoma, skin cancer and prostatic carcinoma.

76. A method for the treatment of drug resistant cancer, comprising administering to an animal in need of such treatment an effective amount of a compound of compound of Formula I:



in which:

the dashed lines indicate optional unsaturation without violating valency rules;

R¹ is hydrogen, (C<sub>1-6</sub>)alkyl or -C(O)R⁶, wherein R⁶ is as defined below, or R¹ is absent when a double bond exists between the nitrogen atom to which R¹ is attached and an adjacent ring atom or R¹ is as defined below;

X¹ is -NR²-, -S-, -S(O)-, -S(O)<sub>2</sub>- or -O-, wherein R² is hydrogen or (C<sub>1-6</sub>)alkyl or is absent when a double bond exists between the nitrogen atom to which R² is attached and an adjacent ring atom;

A¹ is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, or A¹ together with R¹ and the atoms to which A¹ and R¹ are attached forms a fused polycyclic ring system selected from heteroaryl and unsaturated, partially unsaturated or saturated heterocycloalkyl in any case containing a total of 10 to 15 ring atoms, wherein A¹

may be substituted with a group selected from  $-R^3$ ,  $-X^2OR^3$ ,  $-X^2C(O)R^3$ ,  $-X^2OC(O)R^3$ ,  $-X^2C(O)OR^3$ ,  $-X^2SR^3$ ,  $-X^2S(O)R^3$ ,  $-X^2S(O)_2R^3$ ,  $-X^2NR^3R^4$ ,  $-X^2NR^4C(O)R^3$ ,  $-X^2NR^4C(O)OR^3$ ,  $-X^2C(O)NR^3R^4$ ,  $-X^2NR^4C(O)NR^3R^4$ ,  $-X^2NR^4C(NR^4)NR^3R^4$ ,  $-X^2NR^4S(O)_2R^3$  and  $-X^2S(O)_2NR^3R^4$ , wherein  $X^2$  is a bond or  $(C_{1-6})$ alkylene,  $R^3$  is  $-X^2R^5$  wherein  $X^2$  is as defined above and  $R^5$  is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and  $R^4$  at each occurrence independently is hydrogen,  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-6})$ alkyl, wherein each ring within  $A^1$  and  $R^5$  contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from  $(C_{1-6})$ alkyl, cyano, halo, nitro, halo-substituted  $(C_{1-6})$ alkyl,  $-X^2OR^4$ ,  $-X^2C(O)R^6$ ,  $-X^2OC(O)R^6$ ,  $-X^2C(O)OR^4$ ,  $-X^2SR^4$ ,  $-X^2S(O)R^6$ ,  $-X^2S(O)_2R^6$ ,  $-X^2NR^4R^4$ ,  $-X^2NR^4C(O)R^6$ ,  $-X^2NR^4C(O)OR^4$ ,  $-X^2C(O)NR^4R^4$ ,  $-X^2NR^4C(O)NR^4R^4$ ,  $-X^2NR^4C(NR^4)NR^4R^4$ ,  $-X^2NR^4S(O)_2R^6$  and  $-X^2S(O)_2NR^4R^4$ , wherein  $X^2$  and  $R^4$  are as defined above and  $R^6$  is  $(C_{1-6})$ alkyl or halo-substituted  $(C_{1-6})$ alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within  $A^1$  and  $R^5$  may be substituted further with 1 to 2 groups independently selected from  $(C_{1-6})$ alkylidene, oxo, imino and thioxo, with the provisos that only one of  $A^1$  and  $R^5$  is a fused polycyclic ring system;

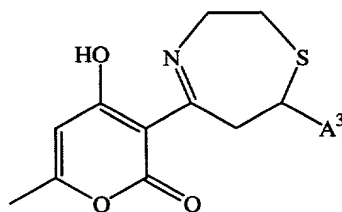
$A^2$  is a monocyclic or fused bicyclic ring selected from heteroarylene or unsaturated, partially unsaturated or saturated heterocycloalkylene containing a total of 5 to 11 ring atoms, wherein  $A^2$  may be substituted with a group selected from  $-R^8$ ,  $-X^2OR^8$ ,  $-X^2C(O)R^8$ ,  $-X^2OC(O)R^8$ ,  $-X^2C(O)OR^8$ ,  $-X^2SR^8$ ,  $-X^2S(O)R^8$ ,  $-X^2S(O)_2R^8$ ,  $-X^2NR^4R^8$ ,  $-X^2NR^4C(O)R^8$ ,  $-X^2NR^4C(O)OR^8$ ,  $-X^2C(O)NR^4R^8$ ,  $-X^2NR^4C(O)NR^4R^8$ ,  $-X^2NR^4C(NR^4)NR^4R^8$ ,  $-X^2NR^4S(O)_2R^8$  and  $-X^2S(O)_2NR^4R^8$ , wherein  $X^2$  is a bond or  $(C_{1-6})$ alkylene,  $R^8$  is  $-X^2R^9$  wherein  $X^2$  is as defined above and  $R^9$  is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and  $R^4$  at each occurrence independently is hydrogen,  $(C_{1-6})$ alkyl or



halo-substituted (C<sub>1-6</sub>)alkyl, wherein each ring within A<sup>2</sup> and R<sup>8</sup> contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C<sub>1-6</sub>)alkyl, cyano, halo, nitro, halo-substituted (C<sub>1-6</sub>)alkyl, -X<sup>2</sup>OR<sup>4</sup>, -X<sup>2</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>OC(O)R<sup>6</sup>, -X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>SR<sup>4</sup>, -X<sup>2</sup>S(O)R<sup>6</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>6</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>4</sup>, wherein X<sup>2</sup> and R<sup>4</sup> are as defined above and R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, and wherein any said heterocycloalkylene, carbocycloalkyl and heterocycloalkyl rings within A<sup>2</sup> and R<sup>8</sup> may be substituted further with 1 to 2 groups independently selected from (C<sub>1-6</sub>)alkylidene, oxo, imino and thioxo, with the proviso that only one of A<sup>2</sup> and R<sup>8</sup> is a fused polycyclic ring system; and

A<sup>3</sup> is a monocyclic or fused polycyclic ring system selected from aryl containing a total of 6 to 14 ring atoms, heteroaryl containing a total of 5 to 14 ring atoms and unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 14 ring atoms, wherein A<sup>3</sup> may be substituted with a group selected from -R<sup>9</sup>, -X<sup>2</sup>OR<sup>9</sup>, -X<sup>2</sup>C(O)R<sup>9</sup>, -X<sup>2</sup>OC(O)R<sup>9</sup>, -X<sup>2</sup>C(O)OR<sup>9</sup>, -X<sup>2</sup>SR<sup>9</sup>, -X<sup>2</sup>S(O)R<sup>9</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>9</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>9</sup>, -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>9</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>9</sup>, wherein X<sup>2</sup> is a bond or (C<sub>1-6</sub>)alkylene, R<sup>9</sup> is -X<sup>2</sup>R<sup>10</sup> wherein X<sup>2</sup> is as defined above and R<sup>10</sup> is aryl containing a total of 6 to 10 ring atoms, heteroaryl containing a total of 5 to 10 ring atoms or unsaturated, partially unsaturated or saturated carbocycloalkyl or heterocycloalkyl each containing a total of 3 to 10 ring atoms, and R<sup>4</sup> at each occurrence independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl, wherein each ring within A<sup>3</sup> and R<sup>10</sup> contains from 3 to 8 ring atoms and may be substituted with 1 to 3 groups independently selected from (C<sub>1-6</sub>)alkyl, cyano, halo, nitro, halo-substituted (C<sub>1-6</sub>)alkyl, -X<sup>2</sup>OR<sup>4</sup>, -X<sup>2</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>OC(O)R<sup>6</sup>, -X<sup>2</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>SR<sup>4</sup>, -X<sup>2</sup>S(O)R<sup>6</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)R<sup>6</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)OR<sup>4</sup>, -X<sup>2</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(O)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>C(NR<sup>4</sup>)NR<sup>4</sup>R<sup>4</sup>, -X<sup>2</sup>NR<sup>4</sup>S(O)<sub>2</sub>R<sup>6</sup> and -X<sup>2</sup>S(O)<sub>2</sub>NR<sup>4</sup>R<sup>4</sup>, wherein X<sup>2</sup> and R<sup>4</sup> are as defined above and R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or

halo-substituted (C<sub>1-6</sub>)alkyl, and wherein any said carbocycloalkyl and heterocycloalkyl rings within A<sup>3</sup> and R<sup>10</sup> may be substituted further with 1 to 2 groups independently selected from (C<sub>1-6</sub>)alkylidene, oxo, imino and thioxo, with the proviso that only one of A<sup>3</sup> and R<sup>10</sup> is a fused polycyclic ring system; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.; with the proviso that when said compound is of Formula II(a):

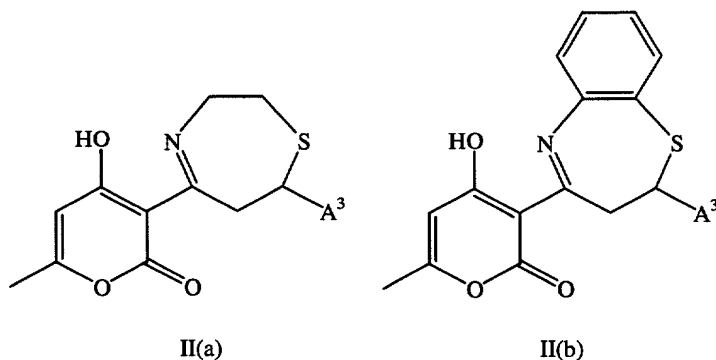


II(a)

then A<sup>3</sup> is other than:

- (a) benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, hydroxy, methyl or isopropyl; and
- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

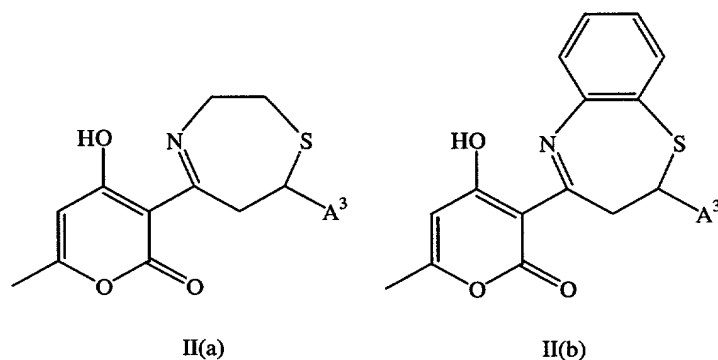
77. The method of claim 76, with the further proviso that when said compound is selected the group consisting of Formula II(a) and II(b):



then A<sup>3</sup> is other than:

- (a) benzo[1,3]dioxolyl;
- (b) phenyl which is mono-substituted by bromo, nitro, hydroxy, methyl or isopropyl; and
- (c) phenyl which is substituted by at least one of Cl and methoxy and not substituted by methylsulfanyl, amino, methylamino and dimethylamino; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

78. The method of claim 76, with the further proviso that when said compound is selected the group consisting of Formula II(a) and II(b):



then A<sup>3</sup> is other than:

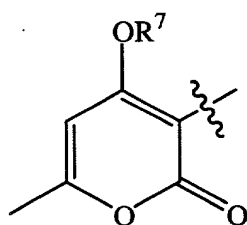
- (a) benzo[1,3]dioxolyl;
- (b) 2,3-dihydro-benzo[1,4]dioxinyl; and

(c) phenyl which is substituted by at least one of bromo, chloro, hydroxy, nitro, methoxy and (C<sub>1-3</sub>)alkyl; or

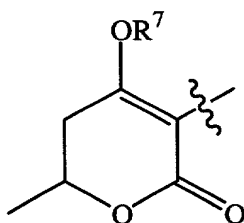
a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof. 1.

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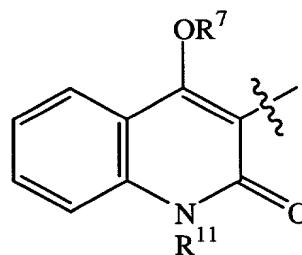
79. The method of Claim 76, wherein A<sup>1</sup> of said compound is a group selected from Formulae (a), (b), (c), (d) and (e):



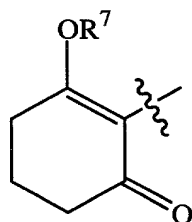
(a)



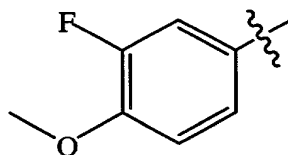
(b)



(c)



(d)

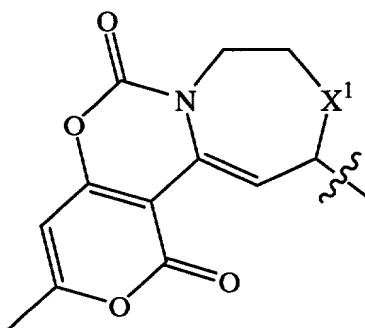


(e)

in which R<sup>7</sup> is hydrogen or methyl, R<sup>11</sup> is hydrogen or (C<sub>1-6</sub>)alkyl and the free valance is attached to A<sup>2</sup>, or

10

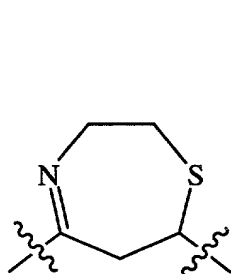
A<sup>2</sup> and A<sup>1</sup> together with R<sup>1</sup> and the atoms to which A<sup>1</sup> and R<sup>1</sup> are attached forms a group of Formula (g):



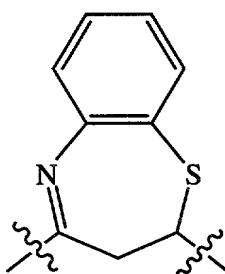
(g)

wherein  $X^1$  is -S- and the free valance is attached to  $A^3$ ; and

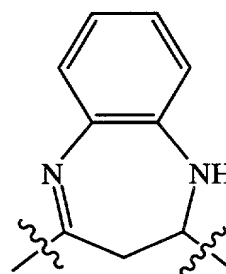
$A^2$  of said compound is as defined above or is a group selected from Formulae (h), (i), (j), (k), (l) and (m):



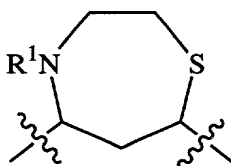
(h)



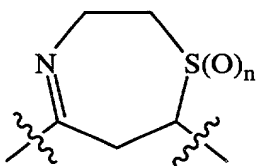
(i)



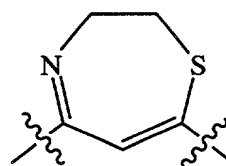
(j)



(k)



(l)



(m)

in which  $n$  is 1 or 2 and  $R^1$  is acetyl or trifluoroacetyl; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

80. The method of Claim 79, wherein  $A^3$  of said compound is phenyl or heteroaryl containing a total of 5 to 9 ring atoms, wherein  $A^3$  may be substituted with a group selected from  $-R^9$ ,  $-X^2OR^9$ ,  $-X^2SR^9$  and  $-X^2S(O)_2R^9$ ,

wherein R<sup>9</sup> is -X<sup>2</sup>R<sup>10</sup>, X<sup>2</sup> is a bond or (C<sub>1-6</sub>)alkylene and R<sup>10</sup> is phenyl or heteroaryl containing a total of 5 to 6 ring atoms, wherein each ring within A<sup>3</sup> and R<sup>10</sup> may be substituted with 1 to 3 groups independently selected from (C<sub>1-6</sub>)alkyl, halo, halo-substituted (C<sub>1-6</sub>)alkyl, -X<sup>2</sup>OR<sup>4</sup>, -X<sup>2</sup>SR<sup>4</sup>, -X<sup>2</sup>S(O)<sub>2</sub>R<sup>6</sup> and -X<sup>2</sup>NR<sup>4</sup>R<sup>4</sup>, wherein R<sup>4</sup> at each occurrence independently is hydrogen, (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl and R<sup>6</sup> is (C<sub>1-6</sub>)alkyl or halo-substituted (C<sub>1-6</sub>)alkyl; or a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

81. The method of Claim 80, wherein said compound is selected from the group consisting of:

4-hydroxy-3-[7-(2-methoxy-4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

2-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

4-hydroxy-3-[7-(4-methanesulfonyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one;

3-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

2-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-3-hydroxy-cyclohex-2-enone;

3-hydroxy-2-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-cyclohex-2-enone;

3-hydroxy-2-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone;

4-hydroxy-6-methyl-3-[2-(2,3,4-trimethoxy-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-5,6-dihydro-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-5,6-dihydro-pyran-2-one; and

3-[7-(2,4-dimethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; or

5 a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

82. The method of claim 76, wherein said compound is selected from the list consisting of:

3-[4-acetyl-7-(2,4-dimethoxy-phenyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-4-(2,2,2-trifluoro-ethanoyl)-[1,4]thiazepan-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

1-[7-(2,4-dimethoxy-phenyl)-5-(3-fluoro-4-methoxyphenyl)-[1,4]thiazepan-4-yl]-ethanone;

4-hydroxy-6-methyl-3-[7-(3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-ethyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

20 3-[7-(1-benzyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3[7-(2-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

25 4-hydroxy-6-methyl-3[7-(3-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3[7-(4-trifluoromethylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-[3-(3-trifluoromethyl-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-[3-(3,4-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-[3-(3,5-dichloro-phenoxy)-phenyl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

5 4-hydroxy-6-methyl-3-{7-[5-(3-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

3-{7-[5-(2-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

10 3-{7-[5-(3-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[5-(4-chloro-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-{7-[5-(2-chloro-5-trifluoromethyl-phenyl)-furan-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-pyran-2-one;

15 3-[7-(4-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-bromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

20 3-[7-(1-benzenesulfonyl-1*H*-pyrrol-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(3-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

25 4-hydroxy-6-methyl-3-[7-(1-methyl-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3-chloro-2-methyl-5-trifluoromethyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

30 3-{7-[1-(2,4-difluoro-benzenesulfonyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;



3-(7-[2,2']bithienyl-5-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-methyl-pyran-2-one;

3-{7-[1-(3,5-dichloro-phenyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

5 3-{7-[1-(4-chloro-phenyl)-1*H*-pyrrol-2-yl]-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl}-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(5-chloro-1*H*-indol-3-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(6-*p*-tolylsulfanyl-imidazo[2,1-*b*]thiazol-5-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(4,5-dibromo-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2-chloro-5-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-5,6-dihydro-pyran-2-one;

4-hydroxy-6-methyl-3-[7-(5-methylsulfanyl-thien-2-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(5-chloro-1-methyl-3-phenyl-1*H*-pyrazol-4-yl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[4-(2,4-dimethoxy-phenyl)-4,5-dihydro-3*H*-benzo[*b*][1,4]diazepin-2-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-2,4-dimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-1*H*-quinolin-2-one;

4-hydroxy-6-methyl-3-[7-(4-trifluoromethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(bis-trifluoromethyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(4-dimethylamino-2-methoxy-phenyl)-2,3,6,7-tetrahydro-  
[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-hydroxy-2-[2-(2,4-diethoxy-phenyl)-2,3-dihydro-  
benzo[*b*][1,4]thiazepin-4-yl]-cyclohex-2-enone;

3-[7-(2,4-dimethoxy-phenyl)-1-oxo-2,3,6,7-tetrahydro-1*H*-1λ<sup>4</sup>-  
[1,4]thiazepin-5-yl]-4-hydroxy-6-methoxy-pyran-2-one;

10-(2,4-dimethoxy-phenyl)-3-methyl-7,8-dihydro-10*H*-2,5-dioxa-9-thia-  
6a-aza-cyclohepta[*a*]naphthalene-1,6-dione;

3-[7-(2,4-dimethoxy-phenyl)-1,1-dioxo-2,3,6,7-tetrahydro-1*H*-1λ<sup>6</sup>-  
[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-  
methyl-pyran-2-one;

3-(7-[2,2']bithienyl-5-yl)-2,3-dihydro-[1,4]thiazepin-5-yl)-4-hydroxy-6-  
methyl-pyran-2-one;

2-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-3-hydroxy-  
cyclohex-2-enone; and

3-[7-(2,4-diethoxy-phenyl)-2,3-dihydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-  
methyl-5,6-dihydro-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual  
stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt  
thereof.

83. A method for the treatment of drug resistant cancer, comprising  
administering to an animal in need of such treatment an effective amount of a  
compound selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-  
[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(4-ethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-  
6-methyl-pyran-2-one;

3-[7-(3-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-  
6-methyl-pyran-2-one;

3-[7-(2-bromo-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]4-hydroxy-6-methyl-pyran-2-one;

3-[7-(2,3-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]4-hydroxy-6-methyl-pyran-2-one;

3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one;

6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

6-methyl-3-(2-*p*-tolyl-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl)-pyran-2-one;

4-hydroxy-6-methyl-3-[2-(4-methylsulfanyl-phenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]-pyran-2-one;

4-hydroxy-3-[7-(4-chloro-2-methoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; and

4-hydroxy-3-[7-(2,4-diethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-6-methyl-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

84. The method of claim 83, wherein said compound is selected from the group consisting of:

4-hydroxy-6-methyl-3-[7-(4-methylsulfanyl-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one;

3-[7-(3,4-dichloro-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-4-hydroxy-6-methyl-pyran-2-one; and

6-methyl-3-[7-(2,3,4-trimethoxy-phenyl)-2,3,6,7-tetrahydro-[1,4]thiazepin-5-yl]-pyran-2-one; or

a *N*-oxide derivative, prodrug derivative, protected derivative, individual stereoisomer or mixture of stereoisomers; or a pharmaceutically acceptable salt thereof.

85. The method of Claim 66, 73, 76 or 83, further comprising administering to said animal at least one known cancer chemotherapeutic agent, or a pharmaceutically acceptable salt of said agent.

86. The method of Claim 85, wherein said known cancer therapeutic agent is selected from the group consisting of busulfan, cis-platin, mitomycin C, carboplatin, colchicine, vinblastine, paclitaxel, docetaxel, camptothecin, topotecan, doxorubicin, etoposide, 5-azacytidine, 5-fluorouracil, methotrexate, 5-fluoro-2'-deoxy-uridine, ara-C, hydroxyurea, thioguanine, melphalan, chlorambucil, cyclophosphamide, ifosfamide, vincristine, mitoguazone, epirubicin, aclarubicin, bleomycin, imitoxantrone, elliptinium, fludarabine, octreotide, retinoic acid, tamoxifen, Herceptin, Rituxan and alanosine.

87. The method of Claim 66, 73, 75 or 83, further comprising treating said animal with radiation-therapy.

88. The method of Claim 66, 73, 76 or 83, wherein said compound is administered after surgical treatment for cancer.

89. The method of Claim 57, wherein said disorder is an autoimmune disease.

90. The method of Claim 57, wherein said disorder is rheumatoid arthritis.

91. The method of Claim 57, wherein said disorder is inflammation or inflammatory bowel disease.

92. The method of Claim 57, wherein said disorder is psoriasis.

93. The method of Claim 57, wherein said disorder is a skin disease.